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JANUARY, 1923

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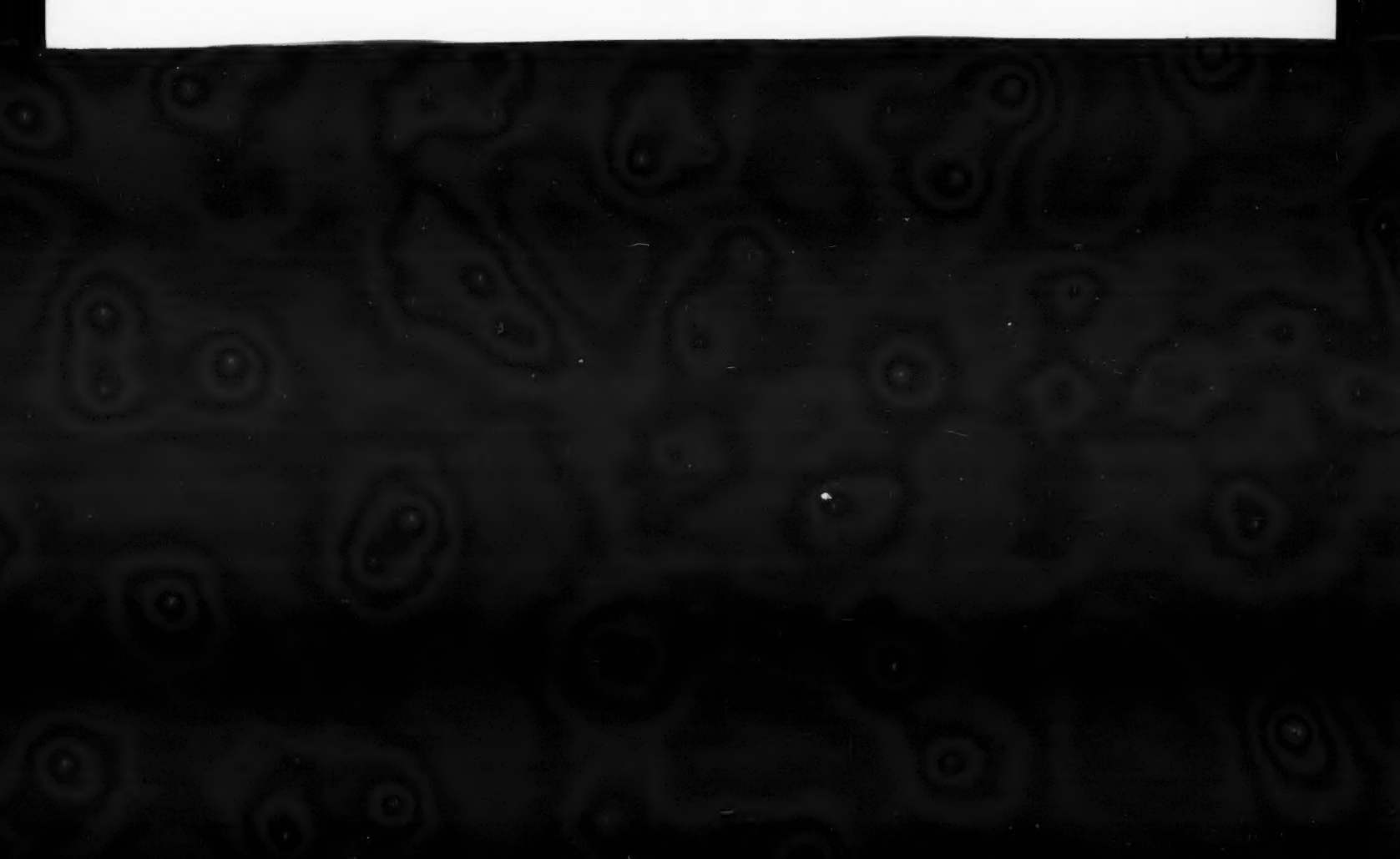

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CONTRIBUTORS TO THIS NUMBER

JAMES M. ANDERS, M. D., Professor of Medicine, Graduate School of Medicine, University of Pennsylvania.

ALBERT EDWARD BOTHE, M. D., Resident Pathologist to the University of Pennsylvania Hospital.

BAXTER L. CRAWFORD, M. D., Associate in Pathology, Jefferson Medical College.

ELMER H. FUNK, M. D., Assistant Professor of Medicine, Jefferson Medical College; Physician in Charge of the Department for Diseases of the Chest of the Jefferson Hospital; Visiting Physician to the White Haven Sanatorium; Assistant Physician to the Pennsylvania Hospital.

CHEVALIER JACKSON, M. D., Professor of Laryngology, Jefferson Medical College; Professor of Bronchoscopy and Esophagoscopy, Graduate School of Medicine, University of Pennsylvania.

LEON JONAS, M. D., Woodward Fellow in Physiological Chemistry, University of Pennsylvania.

HAROLD WALTER JONES, M. D., Instructor in Medicine, Jefferson Medical College; Assistant Physician to Philadelphia General Hospital and Medical Out-patient Department of Pennsylvania Hospital.

RICHARD A. KERN, M. D., Associate in Medicine, University of Pennsylvania; Assistant Physician to the Hospital of the University of Pennsylvania.

ROBERT M. LUKENS, M. D., Chief of Laryngologic Clinic, Department for Diseases of Chest, Jefferson Hospital; Assistant in Bronchoscopic Clinic, Jefferson Hospital; Assistant Demonstrator in Laryngology, Jefferson Medical College; Director of Nose and Throat Clinic, Henry Phipps Institute.

THOMAS McCRAE, M. D., Professor of Medicine, Jefferson Medical College; Physician to the Jefferson and Pennsylvania Hospitals.

T. GRIER MILLER, M. D., Associate in Medicine, University of Pennsylvania; Assistant Physician to the Hospital, University of Pennsylvania.

HENRY K. MOHLER, M. D., Demonstrator of Medicine, Jefferson Medical College.

WILLIAM FREDERIC MOORE, M. D., Laryngologist, Department of Tuberculosis, Philadelphia General Hospital; Assistant Laryngologist, Out-patient Department, Children's Hospital; Clinical Assistant in Laryngology, Jefferson Hospital; Assistant in Bronchoscopic Clinic, Jefferson Hospital.

JOHN H. MUSSER, JR., M. D., Assistant Professor of Medicine, University of Pennsylvania; Physician to Philadelphia General and Howard Hospitals; Assistant Physician, Presbyterian Hospital.

GEORGE WILLIAM NORRIS, M. D., Professor of Clinical Medicine in the University of Pennsylvania; Physician to the Pennsylvania Hospital.

O. H. PERRY PEPPER, M. D., Assistant Professor of Medicine, University of Pennsylvania; Assistant Physician to the Hospital of the University of Pennsylvania.

DAVID RIESMAN, M. D., Professor of Clinical Medicine, University of Pennsylvania; Physician to Philadelphia General Hospital.

JOSEPH SAILER, M. D., Professor of Clinical Medicine, University of Pennsylvania; Physician to the Philadelphia General, the Presbyterian, and the University Hospitals.

TRUMAN G. SCHNABEL, M. D., Associate in Medicine, University of Pennsylvania; Physician, Out-patient Department, University Hospital; Assistant Physician, Philadelphia General Hospital.

ROBERT G. TORREY, M. D., Associate in Medicine, University of Pennsylvania; Physician to Philadelphia General Hospital.

EDWARD WEISS, M. D., Demonstrator of Clinical Medicine, Jefferson Medical College.

C. C. WOLFERTH, M. D., Associate in Medicine, University of Pennsylvania; Assistant Physician, University Hospital; Associate in Cardiac Pathology, William Pepper Laboratory of Clinical Medicine.

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I. HYPERTENSION AND NEPHRITIS

LET us realize first that hypertension in itself is not a disease entity, but a change which occurs with various disturbances. In one group—certainly for a time—we may not be able to find evidence of any actual disease, and to the cases of this group the designation of hyperpiesis, or essential hypertension, has been applied. At present we are not concerned with this question primarily, but with some of the problems of hypertension with nephritis.

It is always interesting to watch an alteration in opinion, and this has occurred to a considerable extent in the views held as to the relation between hypertension and nephritis, and hypertension. I remember a medical meeting in which the view was put forward that hypertension was not necessarily due to nephritis. In the discussion no one agreed with this view; if the patient did not have nephritis he was in the prenephritic stage of it. In the journals recently you have noted articles in which the view is held that in some cases hypertension is primary and the nephritis a secondary affair. This shows that there has been a wide swing of opinion and no doubt some of you are puzzled to know what view of the question is the proper one to take.

First, let us state the problem as concerns nephritis and the changes in the circulation which accompany or result from it.

There are two views held. One may be termed the "mechanical view," which ascribes the primary part to changes in the arterioles or capillaries resulting in compensatory hypertension, cardiac hypertrophy, and vascular changes. These results are to be regarded as due to the effort of meeting increased peripheral resistance. The changes in the smaller vessels are regarded as being responsible for the hypertension. The other view holds that there is some disturbance of metabolism or in the removal of waste products to which the hypertension is secondary. With this some hold the opinion that as regards the changes in the vessels the hypertension is primary and the sclerotic changes secondary. Some go still further and consider chronic nephritis as a consequence of this, in that it follows sclerosis of the smaller vessels secondary to hypertension. It is evident that there is no agreement as to the exact mechanism of the production of the changes in chronic nephritis with hypertension. Does this not suggest that there may be different mechanisms at work?

I have no hesitation in confessing that it is exceedingly difficult to know how best to try and give you a knowledge of chronic nephritis. I fancy that most teachers of medicine are in the same position. The classifications which the pathologist is able to make very properly cannot be used at the bedside. Certainly as regards the disease picture which we call chronic interstitial nephritis or nephritis with hypertension, it is better to regard it as a disease of the whole cardio-vascular-renal system, rather than a renal disorder alone. This is suggestive that factors other than renal are concerned. We must remember that at autopsy in cases of chronic nephritis we usually have a late end-result and that this in the kidney may have been reached by various roads. We cannot assume that the course of events has always been the same.

The study of these patients illustrate some of the problems.

Case I.—The patient, a white female, aged sixty, comes complaining of shortness of breath. She had measles and diphtheria in childhood, but no other infectious disease. During the past four years she has had a good deal of headache at intervals.

For over a year she has had shortness of breath and cough, and at times there have been attacks of severe dyspnea in which she has brought up large amounts of what she describes as white expectoration, sometimes tinged with blood. For two years she has had marked frequency of urination, usually rising four or five times in the night and in the past year she has occasionally passed blood in the urine. Her sleep has been disturbed by attacks of dyspnea. There has been a marked loss of weight; her former average of 230 pounds has fallen to 140 pounds.

The present acute illness goes back about two months. She hurried up the stairs of the elevated line, had sudden severe shortness of breath, and lost consciousness. That night she had a very profuse hemorrhage from the mouth. The blood was in large amount and came up with coughing. She has been unable to lie down on account of dyspnea and has brought up large amounts of thin watery sputum tinged with blood. She has vomited at times.

DR. MCCRAE: Mr. A., what comment do you make on the past history?

STUDENT: The history of cough and dyspnea suggests cardiac diseases, while the frequency of urination with the occasional occurrence of blood in the urine suggests disease of the kidney.

DR. MCCRAE: What significance do you give to the history of the pulmonary hemorrhage and the severe attacks in which she brought up a bloody fluid?

STUDENT: These may have been attacks of edema of the lungs.

DR. MCCRAE: You are right, and such attacks always suggest marked myocardial change. Examine the patient and see what you can determine as to the condition of the heart.

STUDENT: The patient is in bed on a bed-rest, showing well-marked dyspnea. She is somewhat confused mentally and is very restless. There is no marked cyanosis. The heart and pulse-rate is 72. The heart impulse is fairly marked with the apex-beat in the sixth interspace well outside the nipple line. The area of dulness is not increased to the right, but is increased to the left. The sounds are well heard and are clear throughout. The second aortic is somewhat accentuated, but not extremely

so. The vessels show some sclerosis, which is not marked, and the pulse suggests high pressure.

DR. MCCRAE: How would you describe the condition of the heart?

STUDENT: There is hypertrophy of the left ventricle, but the compensation is good.

DR. MCCRAE: Why do you believe that the compensation is good?

STUDENT: The rate is normal, there is no edema of the legs, and no enlargement of the liver.

DR. MCCRAE: Then why is there such marked dyspnea? Before you answer let me say that the dyspnea is very variable. It comes on irregularly and is sometimes more marked than at present. At times it has the appearance of "air hunger" rather than of ordinary dyspnea.

STUDENT: This might suggest that the dyspnea is of renal origin.

DR. MCCRAE: Yes, the condition sometimes carelessly termed "renal asthma." This term is one to be avoided, but it is of interest that the physician who sent this patient to the hospital said that she had asthma. Let us see what the evidence suggests as to the existence of nephritis. The amount of urine averages about 1000 c.c. in twenty-four hours, has a specific gravity of 1.014 to 1.016, contains a considerable amount of albumin, and occasional hyaline and granular casts. She shows some general "edema" as there is fluid in both pleural cavities and in the peritoneum. If this suggests nephritis, which variety would you regard it?

STUDENT: Probably the parenchymatous form on account of the fluid in the serous cavities, the absence of increase in the amount of urine, and the considerable quantity of albumin.

DR. MCCRAE: That sounds reasonable on the evidence which you have, but some important facts have not been brought out. What are they?

STUDENT: The blood-pressure and the blood chemistry findings.

DR. MCCRAE: The blood-pressure is systolic 230 and dias-

tolic 125. The total non-protein nitrogen in the blood is 105 and the urea nitrogen 68. The blood-sugar is 0.1 per cent. The blood-count shows a marked secondary anemia with 3,000,000 red cells. The Wassermann reaction is negative. What bearing has this on the diagnosis?

STUDENT: It shows a nephritis with hypertension and considerable retention of nitrogenous products.

DR. MCCRAE: You can see some of the difficulties of diagnosis in renal disease illustrated in this patient. She shows features in some ways suggestive of both the principal forms, yet it is wise to consider this as an example primarily of nephritis with hypertension. (After the patient had gone.) What changes will you expect the kidneys to show if we obtain an autopsy, for it does not seem likely that she will recover?

STUDENT: I should expect them to be small and contracted. May I ask why the prognosis is so serious?

DR. MCCRAE: The outlook in advanced nephritis with uremia is always uncertain in both directions. There is always the danger of a sudden change for the worse with some serious complication, such as edema of the lungs, and, on the contrary, a patient in the most desperate condition may improve markedly. The ominous factors are that she has not improved to any extent under treatment in the three days she has been in the hospital, the amount of urine has increased very slightly, and the signs of uremia are rather more marked. It has not been possible to give her a sweat-bath, as she showed signs of edema of the lungs when this was tried. There has also been difficulty in purging her. On this last I place particular importance, for when you have difficulty in purging a uremic patient the outlook is always very serious.

As to treatment, this is difficult on account of her condition. She does not co-operate and it is difficult to get her to take fluids. She will only swallow small amounts. It is not possible to introduce much by bowel, and with the tendency to edema of the lungs one hesitates to give fluid subcutaneously. She has taken very active purgatives without much result. Bleeding does not seem advisable on account of the anemia. As to diu-

retics, she is taking theocin, which so far has not had any effect. As her heart is in such good condition digitalis does not seem indicated if one believes that digitalis acts as a diuretic only through its effects on the circulation. Another study of the blood chemistry which is being done today will be of further aid in the prognosis. (This showed non-protein nitrogen 150 mg. and urea nitrogen 104 mg. per 100 c.c.)

I desire to emphasize the fact that this patient presents a picture of renal disease without evidence of any marked cardiac disturbance, or evidence of much arteriosclerosis in the surface vessels. Of course she has marked hypertrophy of the left ventricle, but no evidence at present of myocardial insufficiency.

The patient died rather suddenly two days later. The main findings at autopsy are: Both kidneys are small, less than one-third the size of the normal organ. The capsules are very adherent and leave a granular surface. There is marked atrophy of the cortex. There is marked hypertrophy of the left ventricle, but not of the right. There is no dilatation of the heart and the valves are sound. The heart muscle shows no gross evidence of disease. The arteries show comparatively slight change. The picture is one of marked chronic interstitial nephritis.

Let us discuss some of the problems presented here.

1. **Etiology.**—There is no clue to this and as in many of the cases of this kind we can only surmise. The process in the kidney has been of some duration and of slow advance, and in the absence of marked changes in the vessels the inference is that it was primary in the kidney. Some focus of infection—she had a badly infected mouth—may have been responsible.

2. **What Was the Cause of the Hypertension?** One view explains it as being due to mechanical difficulties; in this case due to the process in the kidneys and not to sclerosis in the arteries generally, and the other that some metabolic disturbance is to blame. You note the greatly hypertrophied left ventricle which is due to overwork so far as we know. Unless we regard this as perhaps due to increased resistance caused by a spasm of the arteries or arterioles it seems reasonable to place the blame

on the kidney changes. My feeling is that in this case the kidney changes are primary and the essential feature. Arteriosclerosis does not seem to play any important part in it.

You may ask why this may not have been a case of primary hypertension with secondary renal changes. It is difficult to disprove this except by the character of the renal findings which are of the type regarded as evidence of primary change in these organs. The absence of any marked arteriosclerosis seems also an important bit of evidence. Certainly the renal changes cannot be regarded as part of a general arteriosclerosis.

3. **What Was the Cause of the Dyspnea and Edema of the Lungs?**—Here we are in difficulties. The history suggests loss of compensation, as edema of the lungs is always suggestive of myocardial insufficiency. Yet during life good cardiac compensation was evident and the gross appearance of the heart muscle is excellent. There is no cardiac dilatation. What part acidosis may have played in causing the dyspnea is a question.

4. The history of hematuria is to be noted. No cause for it was found at autopsy and it is probably an example of the bleeding which occurs occasionally in chronic nephritis. May it have been due to some sudden increase in the already high pressure? The pulmonary hemorrhage suggests passive congestion. There were no signs of this while she was under our observation.

Case II.—This patient presents a picture in some ways like the preceding one whom you saw a few days ago. You see that she is in deep coma and cannot be roused. The face shows some asymmetry and there is evidently facial paralysis, but not of an extreme degree. There is no paralysis of the arms and legs. The patient was brought to the hospital in coma and the history has been obtained from members of the family.

The patient, a colored woman, aged fifty-eight, was in her usual good health until yesterday morning, when she went to a nearby shop and after returning home complained of pains in the legs. A few minutes later she had a convulsion, after which she did not regain consciousness and has been in coma since.

The members of her family are sure that there had not been any change in her usual health evident before the sudden onset.

Her past history is scanty. She is not known to have had any infectious disease. For about three years she has complained of severe headaches. There has not been any cough, dyspnea, or edema. Her digestion has been good and she has not used alcohol. She had 5 children and 1 miscarriage.

DR. McCRAE: Mr. B., what are the striking points in the history?

STUDENT: The sudden onset of symptoms in a patient previously healthy.

DR. McCRAE: Can you state some conditions, injury being excluded, which might account for the sudden onset of convulsions followed by coma?

STUDENT: Uremia, cerebrospinal syphilis, and meningitis.

DR. McCRAE: Mr. C., can you add any other possibilities?

STUDENT: Some form of poisoning.

DR. McCRAE: Which, for example?

STUDENT: Strychnin could cause the convulsions, but not the coma.

DR. McCRAE: It is difficult to suggest any chemical or drug poison which could cause this condition. There are other possibilities which might be considered, but the ones already given are the most probable. We find no signs of meningitis. The blood Wassermann test is negative and the examination of the spinal fluid shows no abnormality, so that syphilis seems unlikely.

The urine shows a specific gravity of 1.017 to 1.026; the amount is impossible to state, as she is incontinent, but it seems scanty; there is a small amount of albumin and a moderate number of casts. The blood chemistry shows non-protein nitrogen 76.5, urea nitrogen 43, and creatinin 3.5 mg. per 100 c.c. The blood-sugar is 0.14 per cent.; there is no sugar in the urine.

The other findings are a slight facial paralysis, irregularity of the pupils, considerable enlargement of the heart to the left, a remarkable amphoric second sound, and marked sclerosis of the arteries, which is of unusual degree. The blood-count is normal as regards the hemoglobin and red cells. There are 15,000 leuko-

cytes, and as she has some fever and signs in the lungs we are suspicious of a beginning bronchopneumonia. The blood-pressure is 235 systolic and 120 diastolic.

DR. MCCRAE: Mr. B., what is your opinion as to the diagnosis?

STUDENT: Chronic nephritis with hypertension and uremia.

DR. MCCRAE: What difference is there in the findings from those in the first patient?

STUDENT: This patient shows very marked arteriosclerosis which the other did not, and the figures of nitrogen retention are not as high.

DR. MCCRAE: There are some points deserving of note. The specific gravity of the urine is rather high for nephritis due to a primary contracted kidney. As a rule such a kidney has lost its power to excrete a concentrated urine. She has a facial paralysis which may be due to a cerebral vascular lesion, although in uremia temporary paralyses are not uncommon, possibly due to local edema. We have no knowledge as to how long the pressure has been high. It may be of short duration. My feeling is that we have in this patient not a primary contracted kidney, but more probably what is sometimes termed an "arteriosclerotic kidney." The absence of edema is against a predominating parenchymatous change. You note the pulsation in the first interspace and the wide area of aortic dulness. These, with the characteristic aortic second sound, suggest dilatation of the aorta. The outlook for the patient is extremely grave and there does not seem much chance for recovery. Death occurred twenty-four hours later.

The autopsy showed a very remarkable generalized arteriosclerosis. It was particularly marked in the aorta, where there were a number of calcified areas. The last 4 inches of the abdominal aorta represented practically a calcareous tube. The left kidney was found with great difficulty and weighed only 10 grams, it was of normal shape, and had only one well-defined calyx. The ureter was small. The right kidney weighed 170 grams, and was somewhat larger than the average kidney. The capsule was stripped off with some difficulty and left a granular

surface. There was one larger scar and several smaller ones on the surface. The cortex in general was narrower than normal and its width was quite irregular.

Comments.—We have here a curious condition of hypoplasia of one kidney, evidently a congenital conditon. I think you will all agree that the other kidney shows much less marked change than we might have expected. In general it suggests the condition termed "arteriosclerotic kidney."

One naturally asks What is the explanation of the sudden onset of symptoms in a patient in apparently ordinary health? The answer is difficult to give. As on admission she had fever and evidence of an early bronchopneumonia, the suggestion might be given that possibly this acute condition had begun before the onset of convulsions. If so, it had not proceeded sufficiently far to make her conscious of illness. As in many similar cases one is in doubt as to what is really responsible for the onset of convulsions.

The condition of unilateral renal hypoplasia has been carefully studied by Dr. Coplin, and I advise you to look up his report.[1] He considers that this form of developmental renal anomaly "predisposes to or renders inevitable some form of nephritis." He regards the abnormality as, in all probability, a defective arteriogenesis. His studies of the structure of the vessels in these kidneys support this view. Patients with such kidneys may reach old age without showing symptoms, but it is easy to understand that when any call for increased activity comes or even slight damage is done, they may become insufficient. In this patient we have no adequate explanation.

Case III.—The patient, a white woman aged fifty, has been under observation at intervals for about three years. Regarding her past history we were never able to learn very much. She was not very intelligent and was unable to give any clear account of illness in early life. She stated that she had always been well until 1916. In this year she states that she suffered from palpitation of the heart with some precordial pain and dizziness. At one

[1] Trans. Assoc. Amer. Phys., 1916, xxxi, 482.

time she had an attack of marked weakness of the left arm, which was evidently temporary, from which she made a good recovery. In 1917 she had an attack of aphasia and with this apparently some weakness of one or both legs, so that she was unable to walk for two weeks. She was unable to give much more of an account than this.

In 1920 she was brought to the hospital in an unconscious condition. There was no history of a convulsion preceding this. She was found by one of her family very pale and weak, and shortly afterward became unconscious. On this admission she had marked edema of the lungs with a full bounding pulse; blood-pressure, 230 systolic and 135 diastolic. She was promptly bled and made a good recovery. She was admitted again in 1921 complaining of headache, some dyspnea, difficulty with her eyesight, and some edema of the feet. At this time her blood-pressure was 275 systolic and 150 diastolic. The eye-grounds showed some sclerosis and tortuosity of the vessels, but not retinitis.

She was admitted again in January, 1922 with very much the same complaints. The pressure at this time was 220 systolic and 130 diastolic. The next admission was in August, 1922, when she complained particularly of dizziness and weakness. She has had a good deal of cough and shortness of breath on any exertion. In addition, she has been somewhat troubled with numbness in the left leg and foot. Apparently at times there has been a certain amount of tingling.

On examination at this time she showed a certain amount of dyspnea and there was some enlargement of the heart, particularly to the left. The heart sounds were clear throughout. The vessels showed considerable sclerosis. The blood-pressure was 250 systolic and 140 diastolic. There was some swelling of the ankles. The patient was in the hospital for about a month. She improved considerably and was discharged in fairly good condition. The hypertension continued throughout, the systolic pressure varying from 240 to 280 and the diastolic from 125 to 150. The phenolphthalein functional test given subcutaneously showed 30 per cent. in two hours; intravenously, 60 per cent. in two hours.

DR. McCRAE: Mr. A., with this history and the findings which have been given, what diagnosis do you feel is suggested?

STUDENT: Chronic nephritis with arteriosclerosis, hypertrophy of the heart, and hypertension.

DR. McCRAE: There is no question whatever that this is a reasonable answer and one in which the majority of people would agree. If you feel that it is justified do not change it when you hear the results of the urinary examinations. During this time in the great majority of the examinations the specific gravity was low, generally between 1.010 and 1.012; one specimen reached 1.016. In a considerable majority of the examinations the urine did not contain any albumin. A few casts were found on two occasions only. No blood-cells were found. The tests showed considerable fixation of the specific gravity. While some would lay great stress on the large number of examinations in which no albumin was found in the urine, I feel that the low and rather fixed specific gravity is of equal or greater importance. The blood chemistry figures were as follows: non-protein nitrogen 41, urea nitrogen 24 mg. per 100 c. c. The blood-sugar was 0.1 per cent. The Wassermann reaction was negative. The blood-count was practically normal.

At the time of discharge of this patient we had considerable discussion in one of the ward classes as to what diagnosis should be made. There was no question about the arteriosclerosis, cardiac hypertrophy, and hypertension, but the point in doubt was whether or not a diagnosis of nephritis was justified, and, if so, whether we could go any further and specify any particular type. Some of you may remember that we finally settled on a diagnosis of chronic nephritis and left it at that. Some perferred to term it "chronic interstitial nephritis," and the possibility of an arteriosclerotic kidney was also considered.

Present Admission.—Having heard the difficulty of the diagnosis on the last admission, we should come to the study of the patient at present with considerable interest. She has been out of the hospital for about three months and has just been readmitted. Apparently she was fairly well for some time after discharge and then began to have a return of the shortness of

breath and cough. She found it impossible to sleep unless she was propped up. Recently she has been troubled a good deal with headache and vertigo.

Examination.—You can see that the patient is dull mentally and the respirations are somewhat labored. The percussion note over the chest is clear, the breath sounds are rather harsh, and she has a great many râles over both sides of the chest. Many of these are whistling and others are coarse and crackling in character. Over some areas there are very fine crackling râles. The heart condition shows nothing very marked except the evidence of enlargement to the left. The sounds are of comparatively good quality and the rate is 88. There is marked arteriosclerosis and the blood-pressure is 225 systolic and 150 diastolic. The urine has a specific gravity of 1.012, contains considerable albumin, and a moderate number of hyaline and granular casts. The blood-count is practically normal.

Later the patient rapidly became worse and died rather suddenly after a very short period in the hospital. On admission the temperature was normal, but soon became elevated, and this, with signs in both lungs, suggested a bronchopneumonia. The blood had not been obtained for the various examinations, as her condition did not suggest such a sudden termination, illustrating again the uncertainty of prognosis in these cases.

The autopsy showed an early bronchopneumonia. Arteriosclerosis is very marked throughout and the aorta and coronary arteries are very sclerotic. Each kidney weighs 110 grams; they are smaller than normal and the capsule is adherent, showing a somewhat granular surface after removal. The cortex is irregular, in some places being much narrowed. The arterioles appear to be unduly prominent. The condition is that which we term an "arteriosclerotic kidney." There is considerable hypertrophy of the heart.

Remarks.—The question as to what actually caused death may be answered in a different way by different men. Probably bronchopneumonia was the immediate cause. However that may be, she was not a good subject for recovery from an acute infec-

tion. What played the greatest part in her long illness and what was the most important factor? My feeling is that the kidney changes were secondary to her arteriosclerosis and it may be a fair probability that hypertension was at least partially responsible for this. But as to how that hypertension was caused we have little on which to base any opinion.

These 3 patients illustrate some of the problems of chronic nephritis with hypertension. In the first the evidence suggests a primary renal change to which the hypertension was secondary. In the second and third cases the kidney changes appear to be part of the general sclerotic process and secondary to it. There does not seem any evidence by which we can say that hypertension was the primary disturbance and that the sclerotic changes resulted from it. Possibly this was the case, but, if so, we are unable to give the cause of the hypertension. You can appreciate the fact that chronic nephritis with hypertension may exist with varying changes in the kidney and a different etiology and progress of events.

II. THE EARLY TREATMENT OF EMPYEMA BY ASPIRATION

The problem of empyema is a borderline one, concerning both the physician and the surgeon. You have seen in the surgical wards many examples of what a long business it sometimes is both for the patient and the surgeon. You have also seen examples of the great difference that an early diagnosis makes in many cases. Every day an empyema is unrecognized may mean a week longer in recovery. We should all be alert to the need of early diagnosis and regard it as a disgrace if a patient is allowed to go with an undiagnosed empyema for any time. This does not mean that the diagnosis is easy, for in some cases it is extremely difficult. Today my object is to show a patient in whom we have had an excellent result without operation and have cheated the surgical side out of a patient—for which I know they bear us no grudge.

First, a few words on the recognition of empyema in lobar pneumonia. Let me emphasize the fact that empyema in lobar pneumonia is nearly always a *complication* and very rarely a

sequel. In other words, the empyema is usually present before the attack of pneumonia is over. It should be our aim to recognize this complication before the pneumonia has terminated, or, if not then, very soon after the drop in temperature. In this latter event it is well to note that here is only one invariable sign of empyema, namely, fever. Everything else has been lacking in my experience in some patients. Of course, this applies to empyema with lobar pneumonia only, which usually adds greatly to the difficulty of recognition. What is said today is to be understood as applying to empyema in lobar pneumonia. The problem is very different from the diagnosis of pleural effusion or empyema arising under other conditions. The consolidated lung adds greatly to the difficulty of diagnosis and the empyema fluid may be in a thin layer.

Inspection.—This does not help us, as there is already decreased expansion from the pneumonia.

Palpation.—This may be of considerable help, as decrease in vocal fremitus may be marked. Naturally other causes must be remembered, such as a plugged bronchus. The area of decreased vocal fremitus may be small and so it may be advisable to use the ulnar edge of the hand in observing it. Tenderness over the site of the empyema is not often present in an early stage.

Percussion.—There may be a change in note, but this depends on the character of the note present over the consolidated lung. If the patient has been under observation before the empyema occurred the change in note may be of value. Of more importance is the sense of resistance, and this, in my opinion, is the most reliable sign in an empyema of any extent. It is better perceived by direct than indirect percussion and the blow should be a very light one. You have to train your finger-tips to appreciate this sense of resistance. Take every chance you can to learn it.

Auscultation.—Two points are of special value—the decrease in breath sounds and an alteration in the spoken voice, which is often very nasal and high pitched. One other point is of interest—the occasional occurrence of râles. These may be heard over an area of chest wall under which there is an empyema.

They are well heard, are usually crackling in character, and their point of origin is of interest. They are usually heard while consolidation is present and probably are produced in the lung and heard through the fluid.

Let us consider the problem in this patient, a white male, aged thirty-nine years. His illness began on January 1st with a sudden severe pain in the back followed by a chill and later by severe pain below the right costal margin. Later there was cough and the severe pain continued. He had fever and was compelled to be in bed from the onset. He was admitted to the hospital on the seventh day of the disease. The crisis occurred within twenty-four hours after admission, the temperature falling to normal and then rising to about 100° F. The history and general appearance suggested lobar pneumonia, which was supported by the physical signs. The leukocytes were 22,000. There was dulness over the middle and lower right lobes with tubular breathing and crackling râles, both in front and behind over the upper part of the dull area. Over the lower part of the right side the vocal fremitus and breath sounds were absent. The voice sounds had a nasal amphoric quality over the lower back and were absent in the lower axilla. The resistance on percussion was much increased. With these signs the house physician, Dr. Ramsay, suspected the presence of fluid. Naturally tapping was indicated to settle the point.

Tapping.—A word as to this is in order. A consolidated lung does not collapse, and so the layer of fluid between it and the chest wall will probably be thin. If the exploring needle is entered a little too far, it goes through the fluid and a negative result is obtained. The effort should be made to introduce the point of the needle just below the parietal pleura. In this case a slightly turbid fluid was obtained, 40 c.c. being removed. The fluid contained a considerable number of pus-cells and pneumococci were found in moderate numbers.

The temperature fell to normal and remained there. The patient felt decidedly better on the following day. On a second tapping, two days later, fluid was not obtained. The dulness decreased rapidly and the patient feels so well that he insists on

going home today, which is the thirteenth day from the onset of the attack of pneumonia.

Remarks.—The question may be asked why the removal of a comparatively small amount of fluid resulted in the rapid absorption of what remained. In the first place, the total amount of fluid was probably not large and the removal of even a small amount may result in stimulating absorption. Might the process have subsided without the removal of any fluid? That is perfectly possible and I know of no way to prove or disprove it. It may be that a condition such as this occurs not infrequently and the patient's resistance is able to overcome it. But in general, from what we know of pus in the pleural cavity, it tends to increase until it is drained. At any rate, if any of us had such fluid in the pleural cavity I am sure we would prefer to have aspiration done on the chance that the infection might subside, as it did in this patient.

We have had a certain number of similar cases. In all the presence of fluid was recognized early—in one on the fourth day of the pneumonia—and following tapping absorption occurred in some, but not in all. These latter went on to the formation of a thicker purulent fluid and subsequently required drainage. Treatment by aspiration is certainly well worth a trial, but it is probably only of value if done early. The possibility of cutting short the course of an empyema is certainly worth every effort to make an early diagnosis. In this do not be afraid to use the exploring needle freely.

CLINIC OF DR. JAMES M. ANDERS

GRADUATE SCHOOL OF MEDICINE, UNIVERSITY OF PENNSYLVANIA

THREE CASES OF CUTANEOUS DISCOLORATION—TWO OF ADDISON'S DISEASE AND ONE OF HEMOLYTIC JAUNDICE

DR. ANDERS: I invite your attention to a few cases of great interest this morning.

Case I.—A. S., aged forty-five; machinist by occupation; married; admitted to the Medico-Chirurgical Hospital October 4th. Both parents died in advanced life of apoplexy. One brother and one sister living and well. Patient had the usual childish diseases. When about eighteen years old he had "a prolonged fever," which might have been typhoid; a couple of years later he had cramps in the abdomen, which came on in the night and lasted until the next day, unless relieved. These recurred at intervals of two or three months until his thirty-third year, and then ceased.

About a year and a half ago he first noticed that he became easily fatigued on exertion and also felt tired on rising in the morning. Six months later he observed that he was growing darker in color over the trunk; this gradually increased in intensity for six months. On admission we noticed the distinct bronzing of the skin, most marked over the exposed surfaces. In addition to the pigmentation his pulse was noted to be exceedingly feeble and the heart action lacked tone. He also suffered from lumbar pains and vomiting, the latter symptom only at long intervals.

In the majority of cases a gradual pigmentation of the skin is the first symptom noted in Addison's disease, although a very slowly increasing asthenia, coming on without apparent

cause, usually precedes. You will notice this man's face expresses more or less apathy and dejection and weakness is profound. The asthenia in this case was the initial feature, and after lasting for six months was accompanied by an increased pigmentary deposit in the skin, being, as is usual, most marked over the exposed portions of the body where the normal pigmentation is pronounced. At present you will observe this is a deep bronze or almost brown hue. The mucous membrane of the lips is also pigmented and there is a dark transverse line near the mucocutaneous junction. As I evert the lower lip you will observe bluish pigment spots on the mucous surface; they also occur elsewhere on the mucosa of the mouth.

The feebleness of the circulation, as already stated, has been extreme in this case, as shown by the small compressible pulse and the blood-pressure readings, averaging about 85 systolic and 50 diastolic. There are no cardiac murmurs and the heart sounds are exceedingly feeble. The temperature is subnormal. His hands are cold and sometimes clammy, due to a feeble circulation. A blood examination showed a marked symptomatic anemia, with moderate leukocytosis—12,000 white cells per cubic millimeter. The metabolic rate was —12.

From the rather unusual history and symptoms which I have enumerated in this case, gentlemen, what is your diagnosis?

STUDENT: Addison's disease.

DR. ANDERS: Yes, the combined presence of the characteristic pigmentation, feeble circulation with low blood-pressure, the marked asthenia, and lumbar pains leave no room for doubt in this case. The gastro-intestinal symptoms are usually more severe than they are in this instance. The only features referable to this tract have been occasional vomiting and lack of appetite. Diarrhea is often a troublesome symptom and is most apt to come on late in the disease. Later on, in the advanced stages, we sometimes observe the patients lying in a somnolent condition; rarely, they exhibit convulsions.

I will next call your attention briefly to the pathology of Addison's disease. In the immense majority of the cases (88 per cent. according to Levin) this uncommon disease is de-

pendent upon a fibrocaseous change of the adrenals. As to the frequency with which destructive lesions of the adrenals occur in morbus addisonii, there is unanimity of scientific opinion, and it should be pointed out that these are found chiefly in the medullary portion, although certain observers contend that the cortical portion is also implicated. The lesion may involve only one of the adrenals, in which case the function of the healthy gland seems to be inhibited. It should ever be recollected that other morbid, non-tuberculous processes in the adrenals, such as carcinoma, sarcoma, and chronic inflammations, may be found at necropsy.

It happens sometimes that in apparently true Addison's disease the adrenals on postmortem present a normal appearance, or, in other words, the function of the adrenals may have been interfered with by some depressing nervous factors. Certain facts that have recently come to light support this theory in relation to morbus addisonii. The solar plexus and semilunar ganglia of the abdominal sympathetic may present a variety of lesions, more particularly inflammatory and degenerative changes. Neisser contends that the symptom, melanoderma, is dependent upon the sympathetic system and that it is conspicuous by its absence in cases of morbus addisonii in which the lesions are strictly limited to the adrenals. Finally, there are those who hold that both the adrenals and the sympathetic ganglia are the seat of pathologic changes.

We went carefully into the history for etiologic factors, but little of importance was found. We noticed that he is a male in middle life, and you will please bear in mind that this disease occurs more commonly in the male than in the female, and most commonly between the fifteenth and fortieth years. This patient, however, has passed that age period by a few years. We have no history of injury in this case, although rarely trauma antedates the development of melanoderma. This man does not give a tuberculous family or personal history. We can only surmise that the lesions which usually characterize the disease are present.

Mistakes in diagnosis commonly arise from assuming that

pigmentation is sufficient to base thereon a decision. Unless marked asthenia with low blood-pressure and gastro-intestinal disturbance are associated with the bronzing of the skin, as in this case, you will not risk a positive diagnosis of Addison's disease.

Other causes for pigmentation, which must be excluded in cases in which one or more of the cardinal symptoms are wanting, are, first, so-called vagabond's disease, by which I mean a condition of the skin produced by the action of filth, lice, and exposure combined. This form of pigmentation closely resembles that of Addison's disease at times. The history in this case, together with the discoloration of the mucous surfaces and the marked asthenia, however, exclude vagabond's disease. If the latter condition is suspected, one should always look at the back for parallel scratch-marks, which can generally be seen. Thorough and oft-repeated bathing with appropriate soap will entirely remove the pigmentation.

Again, in carcinoma of the abdominal organs, particularly where the peritoneum is involved, we may have considerable pigmentation of the skin, but a careful examination of this man's abdomen fails to show anything suggestive of a carcinomatous tumor. There are certain liver conditions, such as the "cirrhosis of diabetes," in which we have a marked deposit of pigment, but here again the mucous membranes are not involved and we do not have the presence of the marked and progressive asthenia and gastric irritability.

In exophthalmic goiter I have seen pigmentation almost as marked as in this case, but here two or more of the following symptoms are present: exophthalmos, tremor of hands, tachycardia, and enlargement of the thyroid gland, all of which are absent in the patient before you. It is to be recollected that chronic progressive hypo-adrenia may in rare instances supervene in the course of Graves' disease. Marine has shown that crippling of the suprarenal cortex may cause increased activity of the thyroid or Graves' disease.

Among other conditions in which the melanoderma may simulate that of Addison's disease are the following: pregnancy

and uterine diseases, in which, however, mere patchy discoloration occurs on the face; melanotic sarcoma and posteruptive staining of syphilitic eruptions. Argyria presents a bluish-gray color of the skin, gives the history of the prolonged use of silver nitrate, and is not accompanied by constitutional symptoms. In argyria the mucous membranes are not involved as they are here.

A diagnosis is an exceedingly difficult problem when this disease occurs in the negro. In such cases we have to rely for diagnosis upon the asthenia, feeble circulation, pigmentation of the buccal mucosa, myalgic pains, and the gastro-intestinal irritability, and thus we can make a reasonably certain diagnosis. The prognosis is exceedingly grave, and, although the mortality has not been reduced, the course of the disease has been prolonged since the advent of suprarenal therapy. The duration varies from one to five years and the termination is invariably fatal. Sometimes we have the sudden, late development of coma and convulsions, but the usual mode of death is by gradual asthenia.

We should resort to all of the usual hygienic measures calculated to increase the strength of the patient suffering from this disease, and instruct such patients to move about slowly and gradually lest syncope come on. They should lie down during each day for several hours. We are giving this patient general tonics, strychnin, and also dried suprarenal gland. I prefer the solid or dried preparation of the whole gland of which the commencing dose is 1 grain three times daily. He is now receiving 3 grains, t. i. d., and at the end of the next five days he will be given 4-grain doses. He expresses himself as feeling a little better since his admission to the hospital.

This patient was shown to the class two weeks later, when the following observations were made:

DR. ANDERS: I bring to your attention for a moment the case of Addison's disease which you saw two weeks ago, simply for the purpose of showing the results of glandular therapy. You will recall that in connection with the treatment I pointed

out the leading theory, which is that the normal secretion of the adrenals, so necessary to tissue metabolism—to life—is greatly diminished in Addison's disease and that we attempt to furnish this by the administration of dried adrenal gland. We give it in ascending doses, and this patient is at present taking 4 grains three times daily. Now, as the result of this treatment, the blood-pressure has been raised, being now 100 systolic and 60 diastolic, while the extremities, instead of being cold and clammy, are warm. The man has more strength and the mental hebetude has been lessened. Finally, as you can see, the skin is growing lighter in color.

Glandular therapy proved of striking benefit in previous cases of my own. Recently the case of the late Dr. Muirhead, which he himself described the course of, up to December, 1920, was reported a second time by Dr. Rowntree (Journal American Medical Association, August, 12, 1922). It was a typical, slowly progressing instance of Addison's disease, in which active suprarenal treatment was of unquestionable value, relieving the asthenia and gastro-intestinal irritability and temporarily clearing up the pigmentation. A word of warning should be uttered against the practice of administering full doses of the gland in the presence of associated tuberculous lesions of the lungs, since in these circumstances copious hemorrhage has been reported where such treatment was instituted.

Case II.—J. M., aged forty-five; Syrian; a retired peddler; married; was first seen October 11, 1922. The family history negative. There is no tuberculosis or malignancy in the family. The patient has had more or less indigestion during the last four or five years and had uncomplicated influenza in 1918. His habits have been good, except for the occasional immoderate use of alcohol. No attention was given to diet prior to the present illness. In August, 1922 the patient began to complain of weakness, which gradually increased. About the same time members of his family noticed that his skin, which had been unusually light for one of his nationality, became darker in color. About three weeks prior to the time he consulted Dr.

H. Leon Jameson, under whose care he had been prior to admission, the digestive symptoms became aggravated following an indiscretion in diet. He complained of vomiting, diarrhea, and indefinite abdominal pains, which lasted for two or three days and have recurred in milder form at varying intervals.

When first seen he had been confined to bed for three weeks on account of asthenia and was able to sit up in bed for a few minutes only at a time. He has had a cough attended with scanty expectoration for several years.

You will notice the distinct darkening of the skin, especially upon the face, hands, and lower portion of the trunk. There are two small patches of leukoderma on the left forearm. The mucous membrane on the lips is dark in spots. The skin is abnormally dry. Sergent's white line is not elicited. There are no palpable lymphatic glands and the thyroid is not enlarged. The mind is clear. The heart is not enlarged, but the sounds are weak, with poor tone; no murmurs or arhythmia. The pulse is weak and very compressible; rate, 82 per minute. The blood-pressure now registers systolic 96 and diastolic 62. At the first examination three weeks ago it was systolic 84 and diastolic 56 mm. Hg.

Examination of the chest reveals slightly increased fremitus and impaired resonance below the left clavicle, and a few persistent râles are audible in this area. The abdomen is flat and no tender areas are found. The nervous reflexes are normal. The temperature has been persistently subnormal.

Repeated urinary examinations have proved negative. Blood count reveals 3,580,000 erythrocytes, 6600 leukocytes, and 67 per cent. hemoglobin. The differential leukocytes count is normal. Wassermann reaction negative. The metabolic rate is —10; this is a usual finding. Two examinations of sputum have failed to reveal the presence of tubercle bacilli.

Since the patient has been under observation he has been taking dried suprarenal gland in increasing dosage in addition to digestants and tonics. His diet has been carefully regulated.

There has been marked improvement, especially in regard to strength. The patient has been sitting out of bed for a week

and took a short walk in the open air yesterday. Digestion is better and the rise in blood-pressure has already been mentioned. I stated in the discussion of the former case that full doses of suprarenal extract should not be given in cases of Addison's disease with associated advanced pulmonary tuberculosis lest hemoptysis be caused as the result of an increased blood-pressure. In this case, however, the lung lesions are slight, and in the absence of any history of previous bleeding, glandular therapy has been cautiously employed.

I have another interesting case to show you. This patient has been in the gynecologic ward and about one week after an operation she was transferred to the medical ward.

Case III.—A. M. S., aged twenty-six; actress; married; childless; her father died of smallpox; her mother of unknown cause. The past medical history reveals the occurrence of the usual diseases of childhood; at thirteen she suffered from tonsillitis and at fourteen she had malaria, with recurrence since then. She has had very troublesome and painful menstruation and has been afflicted occasionally with pain in the region of the liver. One week ago she was operated on, the tubes and ovaries being removed for double salpingitis. No symptoms of sepsis appeared. A saline purgative was administered a few days later and followed by an unusually severe action. The stools were deep green in color, containing a greatly increased amount of bile. A few days later she had a moderately severe rigor and the skin now commenced to take on a yellow hue. This discoloration was not limited to the cutaneous surface alone, but also involved the conjunctiva. The color might be described as of a light lemon-yellow or saffron hue. The urine contains an increased amount of urobilin. A trace of albumin is present and also a few hyaline and granular casts. A blood examination revealed a slight leukocytosis—11,000 per cubic millimeter, erythrocytes 3,500,000 per cubic millimeter; hemoglobin 60 per cent.

DR. ANDERS: Is this a case of catarrhal jaundice?

STUDENT: No.

DR. ANDERS: This is probably correct, although some of the findings are met in simple catarrhal jaundice, *e. g.*, the bile-pigment in the urine and the peculiar lemon-yellow color tint of the skin, although less intense than in that complaint, as a rule. The pulse, however, which is usually slow, is here slightly accelerated, being 80 per minute, although this may be due to the excitement of the hour. Again, the stools contain more than the usual amount of biliary coloring-matter, whereas they are usually dry and clay colored in catarrhal jaundice.

The liver is slightly enlarged and tender. The gall-bladder is probably slightly enlarged, but not palpable. In order to detect the gall-bladder by palpation you must first find the inferior edge of the liver and then pass the palpating finger-tips with gentle pressure along that border.

The diagnosis of simple catarrhal jaundice is readily made as a rule. Its most common cause is catarrh of the duodenum extending itself into the bile-ducts, followed by staining of the skin and conjunctiva after a variable number of days. Symptoms of indigestion are associated, as a rule. In this case there is no history of the ingestion of improper food or of gastric symptoms preceding the appearance of the jaundice. Neither has she caught a "cold." Finally, the history and associated features would seem to exclude simple catarrhal jaundice quite positively.

We sometimes see catarrhal jaundice in kidney and heart disease, but these forms are readily excluded here. Another cause of jaundice is acute yellow atrophy of the liver, but here the liver is increased in size, whereas in acute yellow atrophy it is decreased in dimensions. Cirrhosis of the liver is excluded by the history and associated symptoms as a cause of the discoloration. Might not the icterus have been the result of the poisonous effects of the ether which was used in the operation? Ether sometimes causes a dissolution of the red cells, liberating the hemoglobin in the blood, which usually takes place in the liver and goes to form bile. While this is true, the hemolysis from this cause is insufficient to give rise to jaundice.

You will recall that the past medical history reveals the oc-

currence of repeated attacks of malaria—a disease with which jaundice may rarely be associated. It was therefore thought possible that the rigor which occurred during her stay in the hospital and was followed by slight jaundice might be of malarial origin. The absence of splenic enlargement and failure to find the plasmodium in the blood on microscopic examination, however, excluded that disease as the special cause of the icterus.

Gentlemen, I propound to you another query: Is this not a case of catarrhal cholecystitis?

STUDENT: No.

DR. ANDERS: I am inclined to agree with this opinion. The usual symptoms of cholecystitis are marked prostration, distention of the abdomen, nausea and vomiting, a very sensitive gall-bladder area. Here we have an absence of severe pain over the gall-bladder and of extreme sensitiveness, as well as the other symptoms enumerated. Finally, there is only the slightest degree of fever present.

We have made measurable progress in the solution of this interesting case, the probability being that it is a mild grade of hemolytic jaundice. In favor of hemolytic jaundice in this case I desire to emphasize the cholic stools and absence of bile-pigment in the urine, with increase in urobilin. Again, the intensity of the discoloration is usually less by comparison with that of catarrhal icterus, as is true of this case. This is not, however, an instance of the usual chronic type of anemia with persistent non-obstructive jaundice and decreased resistance to hypotonic salt solution, since the spleen is of normal size and the erythrocytes fail to show diminished resistance, unless it be looked upon as the incipient stage of that condition.

The prognosis must be somewhat guarded, as this case does not seem to be one of simple catarrhal jaundice. The treatment has been symptomatic. She has been taking dilute nitrohydrochloric acid, gtt. v t. i. d., well diluted. Sodium cacodylate has been administered hypodermically once daily, with a view to improving the condition of the blood. Splenectomy is, in my view, contraindicated owing to absence of enlargement

of the spleen and the recent development of the slight icterus. The patient is on a moderately restricted diet, and this is important, especially in febrile cases. She is also taking large quantities of water to flush the intestinal tract and kidneys. We shall watch the case very closely and report the outcome.

Two weeks later the patient was exhibited to the class, when it was noted that all staining had disappeared and the general condition had become practically normal. The blood now gave the following result: erythrocytes 4,200,000, hemoglobin 80 per cent., and leukocytes 9500. The urobilin output had returned to the normal and also the stools as far as their gross appearance was concerned.

CONTRIBUTION BY DR. DAVID RIESMAN

PHILADELPHIA

CORONARY THROMBOSIS. WITH AN ACCOUNT OF THE DISEASE IN TWO BROTHERS AND REMARKS UPON DIAGNOSIS AND TREATMENT

DISEASE of the coronary arteries as such has historically not an ancient lineage. William Harvey describes a case that, as justly maintained by George Dock, may be considered the first recorded example of the affection. The most famous case in literature is that of John Hunter, quite properly appreciated in its relation to angina pectoris by his friend and pupil, Edward Jenner. Parry, a country doctor, to whom Jenner communicated his observations in confidence, also in several instances diagnosed disease of the coronary arteries, and had the satisfaction of having his predictions verified at autopsy. Hunter himself on one occasion found pipe-stem coronary vessels at an autopsy, but did not realize the true significance of his finding. The condition very naturally did not escape the all-observing Morgagni, but not until after Hunter, Jenner, and Heberden did observation and speculation become at all frequent.

While knowledge of coronary sclerosis thus dates back a goodly number of years, that of actual coronary obstruction is of more recent acquisition. In this field experimental studies were a little in advance of clinical observation, a rather unusual circumstance in the history of medical progress. W. T. Porter, Hering, Herrick and Smith, Dock, Libman, Lewis, and Pardee have greatly advanced our knowledge, in part by experiment and in part by clinical investigation.

The causes of coronary occlusion are either embolic or thrombotic processes. The consequences depend upon the size of the vessel occluded, the slowness or rapidity of the occlusion, and the previous state of the heart in which the occlusion occurs. Thrombotic occlusion is more frequent than embolic, and is

conditioned on roughening of the coronary intima by sclerotic or atheromatous disease. If a large vessel is obstructed, death is instantaneous or practically so—the *Minutentod* of the Germans. In animals, after the ligation of a main artery, although death occurs speedily in a majority of cases, life may be maintained for a considerable period.

The coronaries are end-arteries in the sense that there is no anastomosis between them, but a capillary communication exists and is capable of considerable expansion. It is on this basis that one can explain the preservation of life after the slow occlusion of a fairly large branch of the left or right coronary artery. The state of the heart, as I have indicated, is also a factor of moment. Given more or less degenerated myocardium, the reduction of the blood-supply or its complete interruption may be too much, and the heart stops.

Obstruction of a coronary artery leads to infarction of the heart. It is generally held that the infarct is due to a cutting off of the blood-supply, of the nutritive material, but the work of Barcroft has led me to the belief that the death of the tissues beyond the obstruction is due primarily to a deprivation of oxygen, a condition I would designate "histanoxia" (from ἱστός, tissue; *anoxia*, without oxygen). The infarct may undergo softening—myomalacia cordis—with rupture either externally into the pericardium or internally into the ventricular chamber, or an aneurysm may form. The infarct may become organized and constitute a fibroid scar or *Schwiele*. At such cicatricial points the pericardium is usually thickened or adherent, and the heart wall greatly thinned; eventually it may yield, with the formation of an aneurysm.

The clinical features of coronary obstruction are so well illustrated by the cases I have to report that I shall let these cases serve as a general account of symptomatology of the disease.

The first case concerns a man, N. A., forty-nine years of age, a native of Russia, a manufacturer. He consulted me first in 1918, at the suggestion of Dr. M. Goldberg, on account of pain in the left leg which was made worse by walking and by cold weather. During severe paroxysms of pain the

foot would become blanched, and in the patient's own words, "as cold as ice" to the touch. He had never been seriously ill, but had been an excessive smoker until three months before coming under observation.

The only significant finding on examination was total absence of pulse in the left dorsalis pedis, with weak pulsation in both popliteals and posterior tibials. The blood-pressure was 130 systolic, 80 diastolic; the heart and lungs were normal; the reflexes normal; the urine negative. On the basis of history and physical findings I made a diagnosis of endarteritis with intermittent claudication.

I did not see the patient again after the single visit he paid me until his final illness. In the interim he had suffered from attacks of epigastric pain and distention which were attributed to gall-bladder disease by some, to duodenal ulcer by others; under careful dietetic regimen and biliary drainage he seemed to improve.

At 1 o'clock in the morning of December 31, 1921, he was suddenly wakened by a squeezing, cramp-like pain in the middle of the chest. He drank hot water until he vomited, sent for a physician, who applied hot compresses, and gave him a hypodermic injection of morphin. These measures relieved him. On January 4th he had another attack. The next day, while walking leisurely on the street near his home, he was seized with a more diffuse pain in the chest, relieved somewhat by belching. Several other attacks of similar nature followed while walking on the street. In all of them he felt as if he would die. On January 12th at midnight he was seized with violent paroxysms of pain in the midsternal region. He felt, to repeat his own words, "as if a blunt-pointed instrument were being bored into him and were crushing him." The pain did not radiate into the shoulders or arms, but occasionally he would feel a twinge of it in the back. From time to time he eructated gas and passed large amounts by bowel, but without any relief. Dr. Epstein, his attending physician, and Dr. Rosenfeld gave $\frac{3}{4}$ grain of morphin, but saw no effect from it. When I came upon the scene I found, notwithstanding the patient's terrible

agony, that the heart was perfectly rhythmic, the pulse 72, blood-pressure 120 systolic, 80 diastolic. The dorsalis pedis pulse on the left side was absent. The precordial area was hypersensitive to touch. A second dose of ¾ grain of morphin was given twenty minutes after the first, but also without any benefit. Nitroglycerin, benzyl-benzoate, chloroform, and various other remedies were used, but to no avail. From 9 o'clock in the morning until 3 in the afternoon the patient suffered the most intense agony, while the pulse never wavered in its regularity nor did the patient have, strictly speaking, a fear of death. He had, however, a conviction that he would die, and clearly distinguished without prompting between apprehension and a settled conviction—two quite different states of mind. At 3 P. M. he had a convulsive seizure, the heart stopped, but respiration continued for about five minutes after the heart sounds could no longer be heard.

The second case, which I saw through the courtesy of Dr. Clyman and Dr. Rosenfeld, is the following:

M. A., forty-five years old, brother of the preceding patient, had suffered for a number of years from what was called "sciatica." He had also been told that he had diabetes. For the last four or five years he had been repeatedly rejected from life insurance on account of high blood-pressure, but never on account of any urinary abnormality. Postwar industrial conditions had involved him deeply in financial troubles. To this he attributed the fact that he had become an inveterate smoker, contrary to the habits of his earlier life.

On October 5, 1921, while in a department store, he suddenly experienced a queer sensation in the chest, which rapidly changed to one of pain. He succeeded in reaching his factory, and sent for Dr. Clyman, who took him home. The pain increased in intensity. Dr. Clyman, who had in the meantime been joined by Dr. Rosenfeld, did everything in his power to alleviate the man's suffering, giving nitroglycerin, amyl nitrate, morphin, etc. As the blood-pressure, at first 180, had risen to 200, some blood was drawn from the arm, with no other result than a drop in blood-pressure to 170. Finally, chloroform was admin-

istered and gave momentary ease. When I saw the patient the next day the pain had not abated except during short periods. It was chiefly central in the upper chest, to a lesser degree in the precordial area. The patient was panicky, profoundly depressed, and in constant fear of death; his countenance was of a pallid, ashen hue, and expressive of the most intense suffering. The blood-pressure had dropped to 110 systolic, 80 diastolic; the heart was a little enlarged to the left, the sounds very feeble, but regular, 100 to the minute, the temperature 101.4° F. by rectum. The Head zones, though looked for, were not found. The liver was tender to touch.

A careful examination of the legs showed total absence of the pulse in the dorsalis pedis in the right leg. This seemed to point to local obstruction and strengthened our belief that the patient probably had obstruction of the coronary artery. At the end of forty-eight hours, the pain having continued unchanged, it was decided to apply leeches, The blood-pressure by this time had dropped from 200 to 80–84 systolic, 50 diastolic. Râles were present at the bases of the lungs; the color was more ashen than before, the lips a grayish blue. Everything pointed to the most profound collapse and to impending dissolution. Twenty-two leeches were now applied to the precordia, and almost immediately improvement began; despondency and the overpowering fear of death were the first symptoms to disappear. The pressure, however, remained low and the pulse rapid for nearly a week, during which time there was also a little fever, up to 101° F. by rectum. Throughout the attack the bowels remained constipated, the tongue coated, and the breath offensive. The urine was dark and scanty and contained albumin, and on occasions a trace of sugar; the leukocyte count was 8800.

On October 18th, thirteen days after his first attack, the patient was seized with violent abdominal pain during which he again experienced angor animæ—a fear of death. Whether it was an angina abdominis or an enteralgia due to gas could not be determined. On October 31st the blood-pressure was 100, the heart sounds clear and rapid, the heart enlarged both to the right and to the left. The countenance continued to have

a peculiar subcyanotic hue, like that of a man exposed to great cold.

An *x*-ray examination showed moderate enlargement of the heart to the right and left and a little increase in the size of the aortic arch. Electrocardiographic study by Dr. Wolferth revealed irregularity in the spread of the excitation wave in the ventricle and a curve compatible with coronary obstruction, although not identical with those described by Pardee as diagnostic of that condition.

In January, 1922, the patient was taken with a severe attack of influenzal bronchopneumonia, but made a good recovery. His blood-pressure at that time was 120 systolic, 88 diastolic.

The next note was made on April 10, 1922. The blood-pressure was then 144, the pulse 92, the weight had gone up to 164 pounds. The patient felt well, but had not regained his former strength. He could not walk a block without a peculiar feeling in the chest; it was not a pain, and as soon as he stopped it disappeared. A good long breath usually dispelled it. There was no belching or other gastric distress. The heart action was regular, there was no murmur, the second pulmonic sound was a little accentuated, the first mitral sound somewhat muffled. The mucosa of the mouth showed leukoplakia.

On October 28, 1922, the patient had a severe attack of pain in the upper sternal region not radiating to the shoulder, arms, or back; he was extremely weak and had a temperature of 101° F.; the pulse was regular and small; the blood-pressure 126 systolic, 88 diastolic. The heart was distinctly enlarged to the left and showed a gallop rhythm; the left diaphragm was pushed up to the fourth interspace; the abdomen was bloated and tense.

During this attack the fear of death was so strongly upon him that he could not bear to have his physician leave the house. From my records I transcribe a few of the bedside notes:

October 29, 1922: Patient has had a good night, but was seized with a very severe attack of pain this morning. The pulse is 108, the blood-pressure 100 systolic, 75 diastolic. He appears to be in a condition of shock; the face is drawn and of a pale, livid hue. Morphin has had no effect. Leeching advised.

October 30th: The blood-pressure has fallen to 97 systolic, 76 diastolic; the distention is gone, fever continues. Twenty-three leeches were applied. Patient feels greatly relieved.

November 1st: Since the leeching, patient has had no pain. Blood-pressure 76/60. The heart is regular, sounds clear, but distant. The abdomen is soft, the lungs free from râles. There is still a little fever.

November 7th: Although the cardiac pain has ceased, the patient is greatly distressed by a new symptom, seizures of extreme coldness in the legs, starting at the toes and running up to the knees. During these attacks he becomes extremely anxious and must have his doctor with him. After a half-hour he breaks out into a sweat, which is followed by a sense of heat throughout the body, although the legs are still cold. The blood-pressure is 104 systolic, 75 diastolic, the temperature 101° F. Examination of the heart shows a doubtful friction sound just above the ensiform cartilage.

I saw this patient in one of the attacks of cold extremities and found that the legs were indeed extremely cold to the touch, but not changed greatly in color; the pulse in the right dorsalis pedis pulse was absent, as it always had been; in the left feeble. The femoral pulse was good on both sides.

After this symptom had improved I did not see the patient again until the end of December. Contrary to our advice not to leave his bedroom, he insisted upon having his room cleaned, and walked into an adjoining room, and from that into another. Immediately he was seized with a violent attack of paroxysmal tachycardia,[1] accompanied by great anxiety, but not by pain. The seizure yielded promptly, and since then the patient has been in a very satisfactory condition.

During the attacks of pain the urine showed a heavy trace of albumin, had a specific gravity of 1030–1035, and contained a few red blood-cells and hyaline casts.

The blood count was as follows: Red blood-cells, 3,980,000;

[1] In this connection see papers by Robinson and Herrmann (Heart, February, 1921), and by Herrmann, Jour. Missouri State Med. Assoc., October, 1920.

white blood-cells, 8000; hemoglobin, 91 per cent.; polymorphonuclears, 79 per cent.; poikilocytosis and anisocytosis slight.

A study of the blood chemistry gave the following results: Urea, 50 mgm. per 100 c.c. of blood; urea nitrogen, 23 mgm. per 100 c.c.; uric acid, 7 mgm.; creatinin, 1.7 mgm.; chlorids, 462 mgm.

When one remembers that the patient (M. A.) originally had a blood-pressure of about 200 and that in his two attacks it fell to 110 systolic in the first and to 76 in the second, it is evident that some catastrophic change had taken place in the heart. I have no doubt in my mind but there was a thrombosis of a fairly large coronary branch, and that the patient recovered from it either because the thrombus became channeled or because a timely and adequate collateral circulation was established.

As I have already indicated, the obliteration of the dorsalis pedis by thrombo-arteritis is a point in favor of this interpretation.

When the patient began to complain of the peculiar vasomotor disturbance in the lower extremities characterized by coldness and sweating, I feared that he might be developing a thrombotic condition in the abdominal aorta. The mental state accompanying the attacks was very much like that of angina pectoris or coronary thrombosis. However, the condition cleared up so that it cannot have been due to any marked structural change. It may have been a purely vasomotor phenomenon.

From a study of these two cases of coronary thrombosis and others I have seen, as well as from a review of the literature, I would epitomize the characteristic features of the affection as follows:

1. Prolonged severe retrosternal pain with or without radiation—pain more protracted than that of ordinary angina pectoris.

2. Symptoms of collapse with great fall in blood-pressure.[1]

[1] I have recently seen another patient in whom the blood-pressure fell, in what I believe was an attack of coronary thrombosis, from 260 to 125.

3. A blanched leaden hue of the skin, with slight cyanosis of the lips and coldness of the extremities.

4. An overwhelming fear of death or the settled conviction of dissolution.

5. Fever.

6. At times a slight leukocytosis.

7. At times an enlarged and tender liver.

8. Pericardial friction (not constant).

9. Perhaps absent dorsalis pedis pulse.

10. A history of previous attacks which may have resembled ptomain poisoning.

11. At times a characteristic electrocardiogram (Pardee).

Diagnosis.—The differential diagnosis need hardly be discussed, since if the features just given are borne in mind, the diagnosis can usually be made. I may say that the first thought is either angina pectoris or some acute abdominal condition, such as perforation of an ulcer, gall-stone colic, acute pancreatitis, or ptomain poisoning. Rupture of an aneurysm, especially a dissecting aneurysm, may present a very similar picture.

As for the **etiology** of coronary thrombosis, it coincides with that of coronary sclerosis, and about that we know all too little. Syphilis is not a factor of importance, but tobacco is, although, since I have seen the affection in women who did not smoke, it cannot be ranked as the only one.

Treatment.—The first indication is to relieve pain. As shown by the two cases, the usual anodyne remedies and measures may fail entirely. In the second patient those who were witnesses testified to the beneficial effect of leeching. When the man had the second attack he was very glad when I again suggested leeches, for he was sure that it would put an end to the pain.

Other measures of a general character are the use of external heat and careful feeding. All cases that I have seen have complained of gaseous distention at the height of the attack. Malted milk and buttermilk have proved the best foods while the seizure was on. It is not necessary during the attack to enjoin rest—the patient is only too content not to move for any purpose whatsoever. After the attack is over he should remain in bed

for several weeks, and then, to use Allbutt's telling phrase, "he should crawl before he walks." Tobacco should be forbidden for all time to these patients.

A heart that has been the seat of thrombosis and infarction to any marked extent is exceedingly unstable, and any undue exertion may arrest it immediately or cause, as it did in the second patient, an attack of alarming paroxysmal tachycardia. Should the pulse become unduly rapid on the first physical effort, it means that the patient must prolong his rest.

With regard to medication, aside from that designed to relieve pain—for the latter purpose I have also tried papaverin—sodium citrate has suggested itself as a rational remedy on account of its tendency to lessen the coagulability of the blood. I am not sure that it does so when given by the mouth, but I have been in the habit of giving it orally in oft-repeated doses.

The terrific drop in blood-pressure in the cases I have seen has usually brought up for discussion in the consultation the advisability of using digitalis. As a rule we came to the conclusion not to use it, fearing that in view of the great damage to the myocardium it would not do good and might do harm. Instead we have relied upon camphorated oil and caffein sodium-benzoate, and when pulmonary edema was marked, upon atropin.

Although the treatment cannot be considered crystallized, it is well to have a certain definite plan so as to be prepared to act in what is one of the most terrible emergencies conceivable.

BIBLIOGRAPHY

Dock: Notes on the Coronary Arteries, Ann Arbor, 1896, reprint.
Herrick: Jour. Amer. Med. Assoc., 59, 1909; 72, 1919.
Herrmann: Jour. Missouri Med. Assoc., October, 1921.
Lewis: Heart, 1, 1909–10.
Libman: Trans. Assoc. Amer. Phys., vol. xxxiv, 1919, p. 138.
Pardee: Arch. Int. Med., 1920, 26, 2, 244.
Parry: Syncope Anginosa, Bath and London, 1799.
Porter: Jour. Exper. Med., I, p. 46; Jour. Physiol., 1893, 15.
Robinson and Herrmann: Heart, February, 1921.
Smith, F. M.: Arch. Int. Med., 22, 1908.

CLINIC OF DR. GEORGE WILLIAM NORRIS

PENNSYLVANIA HOSPITAL

TUBERCULOUS PLEURISY—CARDIAC ANEURYSM
(A Mistaken Diagnosis)

THE patient whom I have to present to you today, a negro laborer fifty-nine years of age, comes to the hospital complaining of cough and shortness of breath.

For years he has been troubled with colds, which, however, have never been incapacitating until six months ago. At this time, after exposure to inclement weather, he awakened one morning with hoarseness, cough, and sweating. The cough was paroxysmal in character and he thinks that at that time he coughed up "blood-clots." Ever since he has been getting worse, and dyspnea has developed. He has had some shortness of breath for the past ten years, but only upon severe exertion. Lately it has been increasing.

During the last twelve months he has had night-sweats and has lost 17 pounds. He has had pain in the region of the right scapula, increased by coughing and deep breathing. Upon exertion he has noticed some precordial pain, "scratchy" in character, together with vertigo. There has been no edema and no impairment of appetite. For the past two weeks he has vomited practically all he ate, apparently as the result of paroxysmal coughing. There has been no blood in the vomitus. He has had some pain in the back for several years. He has had no other symptoms worthy of note.

Past Medical History.—Sore throat as a child. At the age of fourteen bronchitis. Gonorrhea at fourteen, following which one of his testicles became swollen. Operation was at that time advised, but declined. At the age of twenty-five he contracted lues.

Family history is negative. During most of his life he has worked hard as a stevedore, during the past summer in a very dusty atmosphere. He has been a constant user of alcohol.

Physical Examination.—The patient, propped up in bed, is very dyspneic. He feels no pain at present; is well nourished and well developed; he coughs very frequently.

Pupils are regular and equal; they react sluggishly to light.

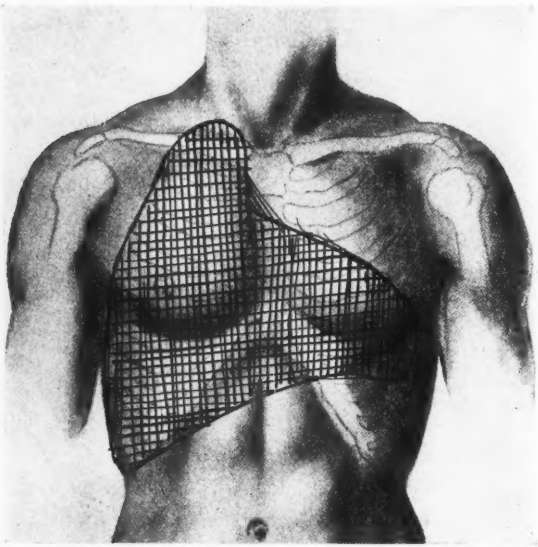

Fig. 134.—The entire right chest is flat on percussion. Expansion absent. Distant bronchial breathing is heard over the upper half of the chest. No râles are noted. The lung is evidently not functionating. The heart is either enlarged or displaced to the left.

Nose is saddle shaped; the exhalations are very offensive.

Inspection of the *mouth* reveals very marked dental sepsis.

Tonsils are large and cryptic; on the left one a small ulcerated (?) area is seen. The cervical lymph-nodes are markedly enlarged, hard, but not adherent.

The veins of the *neck* are distended and expansion of the right *chest* almost absent. Further examination reveals the

physical signs of a massive right-sided pleural effusion (Figs. 134, 135).

Heart.—Cardiac dulness extends 15½ cm. to left of mid-sternal line. The right border cannot be detected owing to flatness of right chest. The rate is increased and rhythm regular. A soft systolic apical murmur is noted. The aortic second sound is faint. The radical arteries are sclerotic.

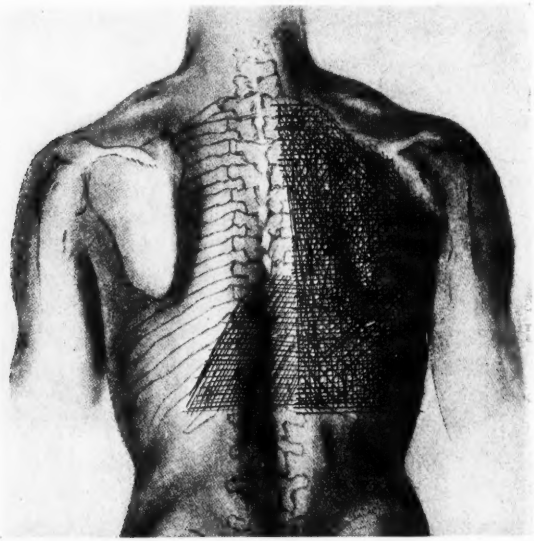

Fig. 135.—Flatness, absent fremitus, distant bronchial breathing over the upper half of the right chest. Grocco triangle on the left.

Abdomen.—The liver is palpable 10 cm. below the costal margin.

Temperature range has been irregular, between 97° and 100° F.

Pulse, 80 to 104. *Respirations*, 32.

Blood: Hb. 78 per cent.; red cells, 4,600,000; leukocytes, 13,240.

Urine, negative.

Wassermann: C+; A−. *Spinal fluid Wassermann:* C−; A−.

A diagnosis of right-sided pleural effusion having been made, and 750 c.c. of hemorrhagic fluid removed from the right chest on October 11th, the heart moved back into position and dyspnea was somewhat relieved. No tubercle bacilli were demonstrated in the fluid.

Four days later, the effusion having rapidly reaccumulated and the patient being very short of breath, another aspiration was performed, at which 250 c.c. of hemorrhagic fluid were removed. Twenty-four hours after this procedure I dictated the following notes:

"Entire right chest anteriorly is absolutely flat, with markedly increased resistance. No vesicular murmur is audible. From clavicle to lower border of fourth rib the breath sounds are feebly but distinctly amphoric. Below this point they become much more feeble and distant and in some areas barely audible, but the character of the sounds which are heard retain the bronchial quality. Heart action is rapid, sounds loud, clear, and booming. Short systolic murmur at apex, with apparent displacement to left. Posteriorly: Entire *right chest* completely flat. Breath sounds at base barely audible, elsewhere they have the quality described anteriorly. *Left chest:* Hyperresonant. Small Grocco triangle apparently demonstrable. Breath sounds exaggerated. Orthopnea is marked. Respirations labored. Complains of 'deadening' pain in front and behind of upper border of the right trapezius muscle.

"*Interpretation.*—The entire right lung is apparently nonfunctioning. Physical signs of massive effusion still persist, either the effusion is loculated and has been only partially withdrawn, or there is an intrapulmonary lesion; neoplasm (?). The neck pain is evidently reflex, resulting from irritation of central portion of diaphragm."

On the same day 1200 c.c. of hemorrhagic serum were removed with symptomatic relief, but without much change in the physical signs. The percussion dulness remained constant except over the upper third and fourth ribs anteriorly, and the breath sounds when audible at all continue to have their

bronchial quality. The chest did not expand and it appeared quite evident that the right lung was not functionating.

Four days later 1750 c.c. of hemorrhagic fluid were removed with some relief of dyspnea, but no great change in physical signs.

x-Ray (Dr. Bowen): "This patient has a massive right-sided pleural effusion, with some mass just to the left of the aortic shadow. The heart and the aorta are also much displaced to the left. I am unable to find any evidence regarding the cause of this, and I do not think that films will give any additional evidence in the patient's present condition."

Dr. John H. Gibbon was asked to see the case in consultation to consider the possibility of establishing permanent drainage of the right chest. He advised against such a procedure, and suggested that, in view of the history and the suspicious Wassermann reaction, the patient be put upon active antiluetic treatment.

Four days later another aspiration (350 c.c.) was necessitated, and again, four days following this, 250 c.c. of bloody fluid were removed, the patient having received rapidly ascending doses of sodium iodid.

You see the patient today in a practically unchanged condition. He still has orthopnea, a harassed and suffering look. The repeated thoracic aspirations have given him only partial, temporary relief. The repeated recovery of blood-stained serum from the pleural cavity points to either tuberculosis or malignancy. The fact that he receives so little relief from aspirations rather favors the latter condition, especially inasmuch as a dense shadow, fluoroscopically, persists over the right lower chest after paracentesis and flatness on percussion does not give place to either resonance (a functionating lung) or not to tympany (a collapsed lung or pneumothorax).

How shall we construe the persistent centrally located shadow which lies in the region of the aorta? The patient is a negro, a stevedore, and states that he contracted syphilis at the age of twenty-five years, and he probably did not carry out treatment very protractedly. This combination—negro,

stevedore, syphilis—very commonly results in aortic aneuryism. Such an aneurysm might be leaking into the pleural cavity, for, as you know, these aneurysms not infrequently rupture into the pleura. Lehman's table, which I have placed upon the blackboard, shows that such rupture occurs in about 7 per cent. of the cases:

RUPTURE (603 CASES)

		Per cent.
Pericardium	150	24.0
Left pleura	101	16.0
Esophagus	53	8.7
Trachea	51	8.4
Right pleura	45	7.4
Left bronchus	38	6.02
Externally	35	5.6
Superior vena cava	31	5.1
Left lung	23	3.08
Pulmonary artery	18	2.09
Mediastinum	11	1.9
Right lung	10	1.6
Right bronchus	8	1.3
Elsewhere (right and left auricles, left ventricles, etc.)	25	4.1

Remember also that the patient has chest pain, cough, thoracic oppression, and vertigo without the usual evidences of cardiac decompensation. With a leaking aneurysm, however, we should expect pure blood, not merely a blood-tinged serum. Furthermore, the fluoroscopic shadow is small, does not pulsate in an expansile manner, and seems to be alongside of, but not a part of, the thoracic aorta.

If the evidence is against aneurysm, how about tuberculosis? The patient has lost 17 pounds during the past year. He has had night-sweats, recurrent attacks of bronchitis, and hemoptysis. As against tuberculosis as an etiologic factor; on the other hand, we have an apparently normal left lung. Now, if the patient had sufficient tuberculosis of the right lung to account for the physical signs, he would certainly have demonstrable involvement of the opposite lung. Furthermore, he has on the diseased side a large pleural effusion plus something else. The picture is not that of pulmonary tuberculosis.

While one cannot be positive regarding the diagnosis, the evidence as I see it points toward malignant disease of the pleura and lung.

(*At the Clinic Two Weeks Later*).—The patient exhibited at this clinic two weeks ago with a provisional diagnosis of pleural and pulmonary neoplasm, shortly afterward left the hospital against advice, only to return, however, two days later in essentially the same condition, but distinctly weaker. Blood-pressure, 120/75; pulse, 124; respirations, 36 Hb., 50 per cent.; red cells, 3,480,000; leukocytes, 14,900. You will note the rapid increase in the degree of anemia. This we attribute to the blood removed from his pleural cavity during repeated aspirations.

Eight days later, after sitting up in bed and asking for food, while being prepared for another aspiration, the patient suddenly threw up his arms, fell backward upon the bed-rest, with a sudden arrest of both respiration and heart action. About 2 drams of bright red blood were exuded from the mouth as life became extinct.

We were allowed to perform an autopsy, at which the following conditions were found:

(Autopsy No. 2589. Hospital No. 3797, November 11, 1922, Dr. John R. Paul.)

Pleuræ.—On opening the chest cavity the right pleura is found to be tremendously thickened and the entire right portion of the chest is occupied by a huge cavity half-full of bloody serous fluid and clotted fibrin. The heart is pushed to the left, extending 11 cm. from the midline. The right border touches the midline. The left lung occupies a position in the superior portion of the left thoracic cavity. The right lung is entirely compressed. It is bound to the right apex by a few old scars, but most of it is present in the mediastinum and covered by a very thick layer of pleura and dense hyalinized adhesions. A large quantity of edematous, hemorrhagic fibrin is found in the chest cavity, which at first was mistaken for some semi-necrotic lung tissue.

Heart.—The heart is not enlarged. It weighs 300 grams. A large cystic tumor is found on the posterior wall of the heart on the superior aspect of the left ventricular wall. It measures 5 x 4 x 3 cm. Its walls are thin, containing calcium deposits, and it contains a small blood-clot. It is also found to be con-

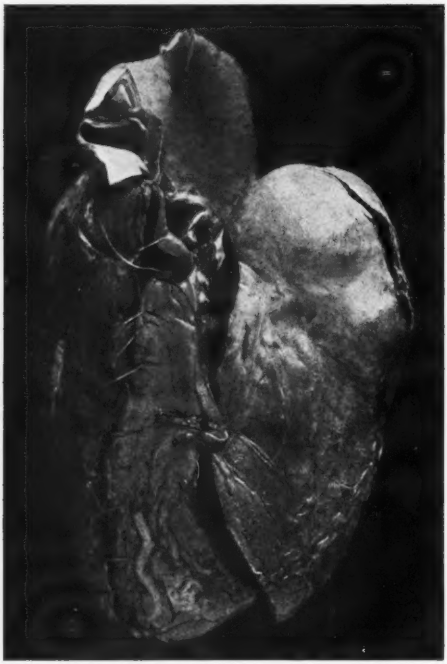

Fig. 136.—Heart, showing calcified cystic mass projecting from the upper part of the left ventricle.

tinuous with the left ventricular cavity, opening by small foramen into this cavity just back of the posterior portion of the mitral valve, evidently representing a saccular aneurysmal formation of the heart wall. The coronary arteries are thickened and tortuous. There are a few patches on the epicardial surface of the heart. The muscle is essentially normal. Valve

measurements: T., 12 cm.; P., 7 cm.; M., 10 cm.; A., 7 cm. (Fig. 137).

Lungs.—Right lung: This is completely atelectatic, due to compression of the old collection of fluid of the right chest,

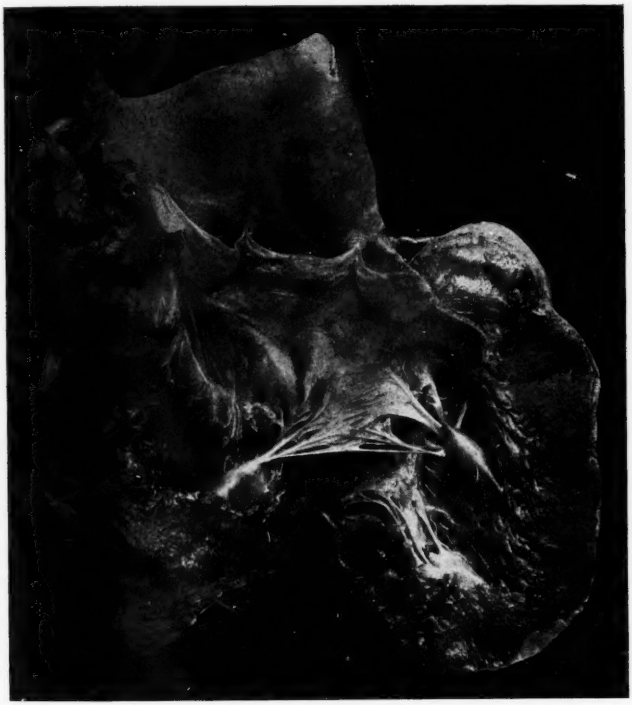

Fig. 137.—Heart, viewed from the ventricle. Mitral, aortic valves, and aorta are normal. An opening from the upper portion of the left ventricle leads into the aneurysmal sac, at the base of which a narrowed, calcified coronary artery is visible.

and has been distorted by pressure upward and medially. Dense old adhesions bind it to the apex and there are a few signs of old caseated tubercles here. About the bronchi and larger vessels there is a dense infiltration of white fibrous tissue and many small areas of fibrous and caseous-like tissue present

in the lung around the hilus and in the hilic lymph-glands. Pus can be exuded from many of the smaller bronchi.

Left lung: Fibrous adhesions due to old tubercles in the apex are present, and there are many old adhesions scattered over the surface. Mild pulmonary edema is present in the lower lobe.

Right pleural cavity: The large cavity described above, which has evidently been formed by a pleural effusion of very long standing, is lined by dense white hyalinized tissue which averages 6 or 7 mm. in thickness. One large adhesion traversing the cavity measures 6 mm. in diameter and contains a vessel in the central portion.

DISCUSSION

Reviewing the case in the light of the autopsy findings, it appears that we should have paid more attention to the history of hemoptysis, night-sweats, fever, loss of weight, and bloody pleural fluid, as evidences of tuberculous pleurisy. And yet, with the absence of tubercle bacilli in the fluid, the rapid reaccumulation after "tapping" and the absence of evidence of intrapulmonary disease, the mistake seems to me more than justified. For even if we had assumed a tuberculous pleuritis productive of such urgent symptoms one should have had a right to expect demonstrable parenchymal involvement.

You will recall that the breath sounds on the affected side when audible at all were always described as bronchial or amphoric. These sounds were evidently transmitted from the bronchi through the pleural exudate, and when this was removed, through the pneumothorax.

The little nubbin lying alongside of the aorta, much smaller than a small fist, densely bound down by adhesions, was all that was left of the right lung. The extreme degree of atelectasis and the density of the adhesions clearly indicate that this lung had not been functionating for years. This is further borne out by the thickness (7 mm.) of the right pleura. You will recall that the patient has suffered from continually increasing dyspnea for ten years. We must assume, therefore,

I think, that this man had been carrying on his work for a long time with literally only one lung.

What of the cardiac aneurysm? What of its etiology? and how great a part did it play in his symptoms?

Cardiac aneurysm usually results from coronary thrombosis, with or without endarteritis. Infarction results; the muscle-fibers soften, degenerate, stretch, and are replaced by fibrous tissue, which ultimately undergoes more or less calcification. The most likely cause in our patient was syphilis. The aneurysm shown you today is unusual, in that it springs from the upper posterior, not the lower lateral, surface of the ventricle. It is, as is usually the case, filled with blood-clot. It probably played a direct part in the patient's death, in that it probably furnished the cerebral embolus which we believe caused the patient's sudden death (partial autopsy; cranial contents not examined).

As is usually the case, the aneurysm was not recognized during life, and figured as an autopsy surprise.

Some years ago I saw in this hospital a negress with a large, actively pulsating mass just outside of the apex impulse, who also had a bloody fluid in the left pleural cavity. The pulsation of the pleural effusion was so great that aneurysm of the abdominal aorta was diagnosed. The autopsy disclosed an aneurysm of the left ventricle.

The subject of cardiac aneurysm has recently been reviewed by Kahn[1], who concludes: "1. Whenever extensive myocardial changes exist, as indicated by the symptoms and by electrocardiographic observations, or when symptoms of coronary thrombosis are diagnosed, myocardial degeneration and thinning of a portion of the ventricle wall should be suspected. 2. In the main, the symptoms of aneurysm of the heart are not otherwise distinctive from the symptoms of the cardiovascular disease in the course of which the aneurysm develops."

[1] M. H. Kahn, Aneurysm of the Left Ventricle, Amer. Jour. Med. Sci., 1922, 163, 839.

CLINIC OF DR. ELMER H. FUNK

JEFFERSON HOSPITAL

SYPHILIS WITH PULMONARY MANIFESTATIONS. THE PROBLEM OF DIAGNOSIS

DR. FUNK: The ward class this morning will be devoted to a consideration of 2 patients studied by members of the section. The first patient has been studied by Mr. A. and Mr. B. Mr. A., will you give us the important points in the patient's history?

STUDENT: P. A., female white, aged twenty-seven years, was admitted to the dispensary service on July 22, 1922. The *family history* is negative. The *past personal history* reveals measles and whooping-cough in childhood; tonsillectomy at eleven years of age; influenza in 1918. She married seven years ago, but has been separated from her husband for several years. One year after marriage, that is, six years ago, she had a miscarriage. She has no children. The *present complaint* dates back to four months prior to admission to the Out-patient Department, that is, in March, 1922. At that time she had pain in the lower right chest which, from her description, resembled the pain of pleurisy. It was sharp, sticking, and aggravated by breathing. After several days the pain lessened and then disappeared, to recur at frequent intervals in a mild form. Shortly after the onset a cough appeared which became productive of a small quantity of yellowish-white sputum. At no time has the sputum contained blood. No night-sweats. At times the voice became husky, which she attributed to the frequent coughing. A few weeks after the onset the patient noticed a swelling over the left upper chest below the collar bone. This swelling became more prominent from day to day, and after several weeks reached a stationary stage which was maintained until she entered the dispensary. At the time of

the first examination she was about 10 pounds below her best weight, she felt in good condition generally, but was annoyed by the cough and dull pain in the side and the worry as to the nature of the lump in her chest.

DR. FUNK: The notes which you have read agree with those which the dispensary physician made at the time of the first visit in July. Were you able to obtain from her any information as to what has happened since that time?

STUDENT: Yes, she states that following treatment the swelling on the chest wall disappeared, the cough and expectoration improved considerably, and she gained about 5 pounds in weight.

DR. FUNK: Before I tell you of our opinion as to the diagnosis at the time of her admission to the dispensary and of the subsequent course under treatment let us hear what Mr. B. has to say about the results of his present physical examination.

STUDENT: The patient is a well-nourished female, no dyspnea, no cyanosis. The pupils react normally. The tongue is slightly coated. The left tonsil is enlarged and diseased. Evidently the tonsils were not completely removed at operation sixteen years ago. The chest is well formed, expansion is slightly limited over the right lower portion. No mass is obvious upon inspection. On palpation I believe I can feel some deep-seated induration over the area, where the patient states the mass was present, *i. e.*, below the inner third of left clavicle. The percussion note is resonant throughout except at the right base posteriorly, where it is impaired from the level of the sixth dorsal spine to just below the angle of the scapula and extending outward to the axilla. The percussion note is less resonant over this area. Auscultation over this same area reveals blowing breath sounds, which are rather distant as compared to the other side; and I can hear no râles. The examination of the heart reveals nothing abnormal. The examination of the abdomen and of the extremities likewise reveals nothing abnormal.

DR. FUNK: Are you reasonably certain, as far as physical signs can determine, that the apices are normal?

STUDENT: Yes, the pulmonary lesion is apparently basal.

DR. FUNK: You have heard the history of the patient to the time of admission to dispensary five months ago and her present physical condition. When first seen the mass to which you refer was situated below the inner third of the left clavicle. It was globular in shape, smooth, firm, painless, and attached to the chest wall beneath the inner margin of the sternum, the clavicle, and apparently extending to but not involving the sternoclavicular joint. The peripheral portion of the mass merged imperceptibly with the adjacent tissues, and the central portion was somewhat softened. The overlying skin was apparently normal and movable over the tumor. No pulsation, thrill, or bruit could be elicited over the mass. From the characteristics of the tumor we made a provisional diagnosis of gumma of the chest wall. The history of a miscarriage and the subsequent findings of a positive Wassermann reaction were corroborative evidence. The signs found in the lungs were those which you have just elicited and, in addition, many coarse squeaks and fine crackling râles over the entire right lower lobe. The pulmonary apices were clear. The sputum examinations were repeatedly negative for tubercle bacilli and mycotic organisms. The basal character of the pulmonary lesion and the negative sputum seemed pretty clearly to rule out tuberculosis. There were other things to rule out. Can you tell us, Mr. C.?

STUDENT: Foreign body.

DR. FUNK: Yes. There was nothing in the history to suggest the inhalation of a foreign body. In this chest clinic we inquire especially in regard to foreign bodies because Dr. Jackson's work taught us how often such bodies are overlooked. We also resort to the *x*-ray, which for both the opaque and non-opaque foreign bodies is indispensable to accurate diagnosis. The *x*-ray revealed no foreign body.

STUDENT: Pulmonary abscess, pneumonic sequelæ.

DR. FUNK: There is no history of a recent pneumonia or of an operation. You will recall that while tonsillectomy is occasionally followed by a pulmonary abscess, the tonsil removal in this patient occurred sixteen years ago. Patients with pulmonary abscess usually have more pronounced local and general

symptoms than this patient had. The amount of sputum never exceeded a few drams a day and was never purulent or foul.

STUDENT: One ought to think of new growth of the lung.

DR. FUNK: This was thought of seriously, especially in view of the mass involving the chest wall. The possibility that the patient had malignant disease of the chest wall and of the lung, and also syphilis, was carefully considered. It must always be kept in mind that a patient may have two, three, or more diseases at any one time. To close one's eyes to further investigation because one disease has been found, is to be guilty of gross carelessness. However, in this patient the absence of dyspnea, which is frequently an early and distressing feature of pulmonary malignancy, the absence of malignant cachexia, and the *x*-ray evidence were against new growth.

In view of the presence of a concomitant lesion of syphilis, and having excluded all other etiologic factors, we assumed that the pulmonary lesion was probably luetic. Dr. Manges, who is conservative in his *x*-ray diagnoses, likewise felt that the lesion was probably leutic. The patient was placed upon intensive antisyphilitic treatment, with the result that the tumor of the chest wall disappeared and the pulmonary symptoms and signs greatly improved, and the general condition of the patient improved. She has occasionally a slight cough and some drawing pain in the side. The physical signs at present are those of a fibroid lesion—the râles which were so numerous before treatment have almost entirely disappeared. The patient whom you have just studied has had intensive antiluetic treatment and continues under treatment, and I believe that the therapeutic response is confirmative of the diagnosis of pulmonary syphilis.

Assuming that the lung lesion is luetic, may we expect it to clear up entirely?

STUDENT: That depends upon the type of syphilitic lesion. In the sclerogummatous form, and especially the form with chronic interstitial pneumonia with bronchiectasis, clearing of the affected lung cannot be expected, although the improve-

ment in some patients is said to be quite striking. In this patient the maximum improvement in the signs has probably been reached.

DR. FUNK: Before we discuss the clinical data on which a diagnosis of acquired pulmonary syphilis would seem warranted, let us pause for a few minutes to recall the gross pathology of the disease. In the secondary stage a bronchitis of varying severity is not uncommon. This is in keeping with the general tendency to mucous membrane involvement in this stage. The lesion is usually transient and of no particular clinical importance apart from the general disease. It is of importance to recognize, however, that in a certain group of these patients there is an associated apical catarrh giving rise to fine crackling râles which may be interpreted as due to a tuberculous lesion. The difficulty of differentiation may be great when it is recalled that the two diseases are not infrequently associated, or when a superimposed syphilis activates an old tuberculous lesion. It may be necessary to suspend judgment until the lues has been controlled by treatment, when the "apical râles" will clear with the associated bronchitis if the signs are due to lues. The clearing up is more prompt and more thorough than that due to tuberculosis activated by lues. I fear that the lack of knowledge of the apical catarrh due to lues has resulted in erroneous diagnoses of incipient tuberculosis. This morning we are interested more particularly in late syphilis of the lung, that which occurs a number of years after the general symptoms have subsided. It most commonly manifests itself as gummata which may occur anywhere in the lung, but usually near the root or in the lower lobes. These may occasionally break down and form small cavities. They rarely form large cavities, as in tuberculosis, and such cavities are rarely found clinically. The gummata may be converted into fibrous tissue, and the resulting contraction and puckering may distort the lung and give rise to considerable bronchiectasis. The gummata of the lung may be latent, and they have been found at necropsy in those who during life gave no evidence of pulmonary disease (Powell and Hartley).

Syphilis of the lung may manifest itself as a diffuse fibrosis. The fibroid lesions of this character, referred to syphilis, do not possess any cardinal characteristics and cannot be distinguished during life from fibrosis due to tuberculosis and other causes. Necropsy evidence may even be inconclusive. Downing notes that this difficulty in distinguishing between the several maladies causing fibrosis makes our necropsy records show so few cases of syphilitic lung disease.

DR. FUNK (to Student): How common is acquired pulmonary syphilis?

STUDENT: I do not know.

DR. FUNK: Accurate information as to the frequency of this form of pulmonary syphilis is not available. Most physicians and morbid anatomists are in agreement as to its rarity. Among 1200 patients referred to the tuberculosis wards of this hospital there were 72 non-tuberculous cases, or 6 per cent., and of these, 4 cases were considered as pulmonary syphilis. Stated in another way, syphilis of the lung was found in 4 instances among 1200 patients who were thought to be unquestionably tuberculous, and in 4 instances among the 72 who were found to be non-tuberculous. Dr. Osler said that it is probable that in clinical investigations many cases either escape recognition or are never treated, while in postmortem records the particular ideas of the investigator as to what constitutes a syphilitic lesion are to be taken into account.

I am not at all in sympathy with those who are willing to diagnose syphilis of the lungs frequently and on scant evidence. I do feel, however, that it occurs clinically more often than the older observers would have us believe, and more often than postmortem evidence would seem to indicate. Is the discrepancy between the clinical and the postmortem frequency contradictory evidence? It may be if we draw an analogy with cardiovascular disease. Certainly not, however, if we draw an analogy with the cutaneous system. I have seen a great many postmortems, but I have failed to see anything like the percentage frequency of lues of the skin which I have seen clinically. May not some of the pulmonary syphilitic lesions clear up antemortem

like the skin conditions? We have been too prone to think of postmortem lues as evidenced only by the gumma or puckered scar. Powell and Hartley, in commenting on Fowlers' findings of only 12 specimens of syphilitic lungs after a careful inspection of museums of the London hospitals and Royal College of Surgeons, state that this museum experience, however, would only in a measure coincide with the clinical experience, since cases recognized will often yield to appropriate treatment.

We will find more cases of pulmonary syphilis than we have in the past in direct proportion to the care with which we study the patients with supposedly unquestioned pulmonary tuberculosis. Tuberculosis is so common that many clinicians have been content with the diagnosis once made, especially if the signs and symptoms suggested advanced disease. Repeatedly negative sputums have not been regarded seriously in the diagnosis. A negative history of lues has been overemphasized. The Wassermann test was not available or was not used. The therapeutic test was never suggested. The Roentgen ray was not used, or used without the aid of a skilled interpreter, or the Roentgen ray gave a picture unlike tuberculosis. And so the patient continued chronically ill with supposed pulmonary tuberculosis.

Now how are we to identify these patients with the rare but nevertheless possible pulmonary syphilis? The following should be kept in mind:

1. The history may point the way; the absence of contact with a tuberculous member of the family or of someone else, the previous condition of health and of habits, the history of an initial lesion with secondary manifestations of syphilis in the past, may stir in the examiner's mind the thought of the possibility of the luetic lesion. The history may be negative, however, as in syphilis elsewhere in the body. The initial and secondary lesions of lues may have escaped attention.

2. The presence of concomitant signs of lues in other organs. In one of our patients the laryngologist called attention to the fact that the laryngeal lesion did not resemble the ordinary tuberculous lesion, and in his opinion it was possibly luetic, whereupon a more careful consideration of the clinical findings

referable to the chest was made, and our diagnosis of pulmonary tuberculosis revised. The patient was placed on antisyphilitic treatment, with the prompt clearing up of symptoms both in the larynx and in the chest. In another the removal of a testicle, supposedly tuberculous, and subsequently demonstrated by the pathologist to be syphilitic, gave rise to a question as to the tuberculous nature of the pulmonary condition. The sputum had always remained negative for the tubercle bacillus, and the patient was placed on antisyphilitic treatment, with prompt improvement.

3. Tuberculosis is a disease which involves at first the apices of the lungs and spreads therefrom. A primary basal lesion is extremely rare. Among several hundred consecutive necropsies I have not seen a single case. Lues, on the other hand, usually involves the hilus areas or the bases, and the presence of such a lesion strongly suggests a non-tuberculous lesion, and among these one finds the cases of lues. That involvement of the apices may occur is illustrated by the case reported by Hoffman, in which a bilateral lesion involving extensively the tops of the lungs was found.

4. Advanced tuberculous patients and those with persisting purulent sputum due to tuberculosis practically always have bacilli in their sputum. Conversely stated, whenever the sputum of a patient with symptoms and signs of advanced disease is repeatedly negative for tubercle bacilli, it is wise to think of something else. And in this group is pulmonary syphilis.

5. The positive Wassermann reaction means syphilitic infection, recent or old, and fairly certainly not controlled. A positive Wassermann reaction does not mean that a pulmonary lesion is of necessity syphilitic. The two infections may coexist —pulmonary tuberculosis and syphilis without lung involvement. In fact, this association is rather common. The Wassermann reaction assumes diagnostic importance in regard to the pulmonary lesion when all the tests for tuberculosis are negative.

Keilty reported in 1916 a case of syphilis and tuberculosis in the same lung. The patient, a colored male of twenty-three

years, with distressing cough, profuse expectoration, and loss of weight, showed physical signs pointing to infiltration and cavity of the lower left lung. Tubercle bacilli were absent from the sputum. At necropsy, syphilis in the form of chronic interstitial pneumonia with bronchiectasis, and tuberculosis in the form of miliary and conglomerate tubercles with caseation were found in the left lung, and tuberculosis almost alone was found in the right lung. Both the tubercle bacillus and the Treponema pallidum were demonstrable in appropriately stained preparations.

6. The Roentgen diagnosis of lung syphilis has recently come into prominence. Time will not allow of our discussion of the value of the *x*-ray as expressed by various authorities. The *x*-ray is a help in diagnosis. It is "a bit of evidence, but not a verdict." It will help us to eliminate foreign body, etc.; to locate the lesion, etc.

7. The response to antisyphilitic treatment. No known drug can do in pulmonary tuberculosis what arsphenamin, mercury, and the iodids can do in pulmonary syphilis. Furthermore, these same remedies are without influence in the tuberculous lesion unless there be an associated syphilitic infection, in which event the treatment clears up the latter infection and gives the body a better chance, so to speak, to attack the former, which it usually does, but the lung lesion does not improve so promptly as in pulmonary syphilis alone. As a matter of fact, the iodids are of diagnostic value. The prompt manner in which they help clear the luetic lesion is not seen in tuberculosis. They may not influence the pulmonary tuberculous lesion, but in my experience there is no question of their deleterious effects in some cases. Brambilla reports the interesting observation of a supposedly tuberculous patient recovering following mercurial inunctions intended for a syphilitic patient in an adjoining bed.

Finally, and to repeat, I hold no brief for the great frequency of lung syphilis which some would have us believe. I do believe, however, that among chronic lung patients we will find some few who suffer because of a luetic lesion in the lung. I believe

that among the non-tuberculous group those comprising the mycotic infections, chronic abscess, tumor, pneumokoniosis, etc., syphilis is no mean contender. In these syphilitic patients we are enabled, as Dieulafoy states, to score a therapeutic success, for we can sometimes restore health in a few weeks or in a few months to patients who appear to be in the last stage of pulmonary tuberculosis.

DIABETES AND TUBERCULOSIS. THE PROBLEM OF TREATMENT

DR. FUNK: The second patient has been studied by Mr. C. and Mr. D. Mr. C., will you give us the important points in the patient's history?

STUDENT: Mrs. S. L., aged sixty-seven years, white, was admitted to the wards of the Chest Department on October 13, 1922. Her *family history* reveals the following: Father died at seventy-three years of paralysis, mother died at eighty-two years following a "heat-stroke." Both parents had excellent health until shortly before their terminal illnesses. The mother was obese. Two brothers and 4 sisters are living and well, except 1 sister, who has diabetes. All the brothers and sisters are much overweight for their height, averaging about 200 pounds. The patient's *past personal history* reveals the usual childhood diseases and a curetage in 1913. Menopause occurred at fifty years. She has been married forty years. Her 2 sons have died, one in 1919 and the other in 1922, from a "general breakdown." The patient's husband has always been a healthy man.

The *present illness* began about four years ago, when she began to lose weight, and this has been progressive to the present time. The patient states that for thirty years prior to four years ago she weighed an average of 205 pounds. She has always consumed considerable quantities of water, but during the past year the thirst at times has been unquenchable. The appetite has been poor as a rule. Constipation has been a distressing symptom for many years. There has been no noticeable polyuria. The sorrow caused by the death of her 2 sons in 1919 and 1922 respectively is the reason which she gives for her loss of weight and strength. In January, 1920, that is, about one year after she began to lose weight, she contracted a "bronchitis" which would not yield to treatment. Since this time she has coughed more or less constantly, although with varying severity. At times the cough and expectoration would almost

entirely clear up, and then return. At no time has the sputum contained blood. The present distressing cough has been constant since November, 1921. For about two months prior to admission night-sweats have occurred with distressing frequency.

DR. FUNK (to Student): Mr. D., will you give us your findings upon physical examination?

STUDENT: The patient is of fair color and somewhat emaciated. The skin over the body is dry and appears unusually redundant. The face is slightly flushed. No cyanosis or dyspnea is present. The pupils react normally. The tongue is slightly coated. A few palpable glands are found in the neck. The chest is rounded, the expansion is generally limited, especially on the right side. The percussion note over the right side from apex to the third rib in front is high pitched and tympanitic in quality, and posteriorly is distinctly less resonant from the apex to about the angle of the scapula. Over this area there are numerous coarse and fine râles. There are a few scattered squeaking râles over the left lung posteriorly.

The heart shows nothing of special note except some weakness of the sounds. The abdomen is soft, the wall relaxed and redundant. The spleen is not palpable. The extremities show nothing of special note except the evidence of emaciation.

DR. FUNK: The final opinion as to the diagnosis should be reserved in every patient until one has had time to consider not only the history, symptoms, and signs but also the sputum findings, the blood and urine examinations, the *x*-ray, etc. However, at this point, have we sufficient data upon which a reasonably accurate tentative diagnosis might be made?

STUDENT: The history of chronic cough and expectoration with loss of weight, the signs of a moderately advanced pulmonary lesion involving the tops of the lungs, would seem to be rather strong evidence favoring tuberculosis.

DR. FUNK: Yes. Is there not something else of considerable significance in the patient's history which ought to direct our attention to the possibility of another disease as well?

STUDENT: She tells us that she has diabetes.

DR. FUNK: No, that is not the point. Is there anything in her history which ought to make you think of the possible presence of diabetes irrespective of her statement as to its presence?

STUDENT: The history of obesity in the mother and 6 brothers and sisters, the fact that 1 sister has diabetes, and the loss of considerable weight which seems to have antedated the development of the symptoms of pulmonary disease would suggest the presence of diabetes.

DR. FUNK: Quite right, and I would add the patient's statement that she was a large water drinker for many years and at times was quite annoyed by the thirst. You should always suspect the presence of diabetes in families with obesity. Mr. C., will you tell us of the laboratory studies?

STUDENT: The sputum was found to contain many tubercle bacilli. The urine collected during the first twenty-four hours of the hospital stay showed 5.5 per cent. sugar; and subsequent twenty-four hour specimens during six days varied from this down to 0.4 per cent. the day before it disappeared as a result of dietetic restrictions. The blood-sugar shortly after admission to the hospital was 212 milligrams per 100 c.c. of blood. The Wassermann test, which is done routinely in the wards, was negative. The *x*-ray confirms the findings of the physical examination. There is considerable thickening about the hilus, particularly on the right side. The right upper lobe and upper half of the right lower lobe show an increased density, with accentuation of the linear markings. There is apparently considerable infiltration of the lung, but no cavity formation.

DR. FUNK: You can now tell us with some certainty as to the diagnosis?

STUDENT: Yes. Pulmonary tuberculosis and diabetes.

DR. FUNK: Before we discuss the treatment of a patient with these two diseases let us pause to consider some elementary concepts of the two diseases. Diabetes develops, as a rule, in a person who is overweight for his age and height. Diabetes, as Dr. Joslin puts it, is often the penalty of obesity, of overeating, and underexercising. Diabetics usually have an excellent appetite and good digestion, but an inability to utilize carbohydrates,

with the resulting hyperglycemia, glycosuria, and other symptoms of the disease. Diabetics also have disordered protein and fat metabolism, and the inevitable result of the uncontrolled disease is wasting, reduced resistance to infection, coma, and death.

Pulmonary tuberculosis, on the other hand, develops, as a rule, in those who are underweight for their age and height. Undernourishment and overexercise, that is, faulty dietary factors and fatigue, play important etiologic rôles. The appetite and digestion are frequently impaired. There is no reduction in the ability to utilize carbohydrates, protein, and fat, but the result of uncontrolled tuberculosis is like diabetes in the wasting, weakness, and death.

At first glance it would seem rather queer that these two diseases with such diverse origins should ever be associated. They are more commonly associated than is generally considered. The question frequently propounded is: Which disease occurred first in the individual? It is our opinion that in practically all cases diabetes is the initial disorder and the active tuberculosis a subsequent development. Whether a latent tuberculosis is activated by the diabetes, or whether reinfection occurs as a result of disturbed metabolism, does not particularly concern us at this place. It is to the point, however, that the diabetes probably determines in most instances the development of tuberculosis in the person in whom both are found to be present. In the patient which we are studying this morning the diabetes, in all probability, came first and then the tuberculosis.

DR. FUNK (to Student): The association of these two diseases presents a particularly vicious combination to treat. At the outset one is confronted with *the problem of the diet*, and these questions arise: (1) Should we ignore the diabetes, as was the common practice in the past, and treat the tuberculosis? or (2) Should we ignore the tuberculosis and endeavor to control the diabetes?

STUDENT: The antituberculosis régime could be used with advantage in this patient.

DR. FUNK: That is true with regard to rest in the fresh air, etc., but what is your answer to the question of the diet?

STUDENT: The diabetes should be given the first consideration as far as the arrangement of the diet is concerned.

DR. FUNK: Quite right. If our elementary concepts of the two diseases are correct, it would seem logical to give the treatment of the diabetes our first consideration, applying, at the same time, such measures as rest and fresh air, which are not incompatible with a strict diabetic treatment. Experience has justified the attitude of ignoring, for the time being, the tuberculosis, as far as the diet is concerned, and of attempting to correct the hyperglycemia and render the urine sugar free by the application of either the fasting method of Allen, of the gradual reduction method of Joslin, or even the high fat and low protein diet of Newburgh and Marsh. The inevitable result of the application of these dietetic restrictions is a loss of weight, which to one interested in the tuberculosis is quite disconcerting. Our reply to those who are concerned with this loss of weight is that it would inevitably occur if the diabetes was not controlled. Following such a loss of weight from treatment it is possible to have a patient gain in weight to an extent that is not possible in any other way. In other words, following dietetic restrictions there is a gain in the patient's ability to utilize carbohydrates and properly metabolize fat and proteins, and with this improvement a chance not only for a gain in weight, but an increased resistance to further extension and activity of his tuberculosis. *Increased resistance to the progress of the tuberculous infection is a more important result of antidiabetic treatment than ability to gain weight.* In that particular group of tuberculous patients in which diabetes is present, weight increases have less significance, as far as the improvement of the tuberculous condition is concerned, than in others, and this is in keeping with our knowledge of the prognosis of diabetes. The undernourished diabetic keeps well longer than one who tends rapidly to put on weight. The tuberculosis will improve even though there is no considerable gain in weight if the diabetes remains under control at a given weight.

DR. FUNK (to Student): You will notice from the temperature chart that there has occurred an improvement as far as the

tuberculosis is concerned. The activity of the disease has distinctly lessened. The local symptoms of cough and expectoration have greatly improved. The signs in the chest have not changed except for a lessening of the number of râles. You will recall how often I have emphasized the slowness in the improvement of signs as compared to the symptoms in patients who are recovering from pulmonary tuberculosis. This improvement, as far as the pulmonary tuberculosis is concerned, is being accomplished in this patient by controlling the diabetes. The patient was first rendered sugar free by the diet reduction method of Joslin, with one day of fasting. When feeding was resumed the 5 per cent. greens were given at the start, increasing the amount and strength of carbohydrate foods daily. Protein was added simultaneously. At first, 1 and then 2, 3, 4 eggs, lean meat, until an amount of protein was reached sufficient to maintain nitrogen equilibrium, *i. e.*, 1 gram per kilogram of body weight. Fat was added to the diet from the start. The fat addition was made with a due regard for the maintenance of a fatty acid glucose ratio of not exceeding 1.5 : 1.

We have been able to reach a diet of about 1900 to 2000 calories (approximately), which is adequate for her. She remains sugar free. The hour is drawing to a close and we must leave for another time a discussion of those principles underlying the modern dietetic treatment of diabetes. Such treatment does not differ when in the given patient there is an associated pulmonary tuberculosis unless that patient is obviously hopelessly advanced with the tuberculous disease. Let me impress you today with the importance of recognizing the necessity of treating the diabetes, and if this can be done effectively, the patient has a much better chance to successfully combat the tuberculosis.

CLINIC OF DR. JOSEPH SAILER

PHILADELPHIA GENERAL HOSPITAL

TUMORS OF THE MEDIASTINUM

TUMORS of the mediastinum may be divided into two groups from the standpoint of diagnostic convenience: the aneurysms and the others. This classification is far from scientific, but meets the needs of practical diagnosis. Aneurysms are sufficiently common and the diagnosis may be easy, depending upon the size and position of the aneurysms and the character of the symptoms. The other mediastinal tumors are probably not so rare as is commonly supposed. Doubt always exists in the mind of the clinician whether the diagnosis is correct or not, and when the diagnosis is made there is a strong feeling of disappointment because the prognosis is usually grave. The cases herewith reported have many points of resemblance and are sufficiently interesting to justify a record.

CASE I

Mrs. A. O. B., sixty years of age, a widow, was first seen in March, 1914. She complained then of insomnia and pain in the joints. An ovarian tumor had been removed at the age of forty-six. For several years she had complained of a condition diagnosed as rheumatism of the throat. She had suffered in the past from sick headaches. For some years she had dyspnea on exertion and palpation of the heart after meals. She had a sense of weight and pressure in the epigastrium, especially at night. She was obliged to pass urine several times each night, and had some swelling of the hands and feet through the day, especially in the morning. She slept poorly, being frequently wakened during the night, and having difficulty in getting to sleep again. The pain in the joints and swelling in the hands had lasted then for six or seven years. Her weight was 145 pounds, the heaviest she had

ever been. There was a loud systolic murmur heard over the heart and transmitted into the vessels of the neck. The lungs were normal. The descending colon was palpable and very tender. The elastic resistance on the right side of the abdomen was greater than on the left; otherwise the abdomen was normal. There were some of the characteristic changes of chronic arthritis, especially in the hands. The blood-pressure was 179/87. The hemoglobin was 68 per cent. The red blood-cells were 3,550,000. The white blood-cells, 9600. Differential count: Polymorphonuclears, 79 per cent.; lymphocytes, 10 per cent.; large mononuclears, 7 per cent.; transitionals, 2 per cent.; basophils, 2 per cent. The urine contained a faint trace of albumin, but was otherwise normal. At this time there was no tracheal tug. Slowly the patient improved and the pains disappeared. Sleep continued poor, and she remained moderately anemic. The hemoglobin ranged between 65 and 60; red blood-cells, 3,500,000. Blood-pressure varied from 160 to 170 systolic and from 65 to 85 diastolic. This continued for a period of five years. In November, 1919 she had an attack of sudden dizziness during which objects whirled about, and this was repeated several times. No definite cause could be ascertained for the attacks, which occurred for several months. The physical examination at this time revealed a vigorous pulsation in the suprasternal notch and a very strong tracheal tug. There was also slight enlargement of the heart dulness; a greatly accentuated second aortic sound and a loud systolic murmur heard over the whole heart, but most distinctly at the aortic cartilage, both were well transmitted to the vessels of the neck. At this time the blood-pressure was 165/88. Red blood-cells, 4,700,000; white blood-cells, 11,000.

The patient was referred immediately to Dr. H. K. Pancoast with a diagnosis of some abnormal condition in the superior mediastinum. The report of his examination is as follows:

"The examination of the chest is somewhat of a puzzle to me. The heart is apparently enlarged to the right. The trachea is decidedly deviated to the right. In the anteroposterior direction I thought she had some enlargement of the first portion of the

arch of the aorta, but there was no marked pulsation, and an oblique view seemed to show the arch to be normal in width, but with a shadow beneath it. The appearance was very suggestive of a mediastinal mass. She was very nervous at the time of the

Fig. 138.—Case I.

fluoroscopic examination, and I want to go over her again, but the appearance suggests something decidedly wrong in the mediastinal region" (Fig. 138).

After the second examination he writes: "I feel reasonably

certain that the abnormal appearance is not due to an enlargement of the aorta. There seems to be something under the arch pushing it out." At this time blood was taken for a Wassermann, which was negative; nevertheless, the patient was placed on potassium iodid. The pulse was slightly Corrigan. The blood-pressure in the right arm was 140/90; in the right leg, 193/125. After taking this I felt that the possibility of an aneurysm associated with insufficiency could not be as definitely excluded as it had seemed at first. However, the second *x*-ray led Dr. Pancoast and myself to decide that the most hopeful treatment in this case would consist of deep *x*-ray applications to the interior of the chest. Dr. Pancoast proceeded to carry out this idea using cross-fire radiation. Until this time the patient had had an intolerable cough that disturbed her sleep and during the day was constant. The throat was dry and she felt a constant tickling in the throat. It did not have the brassy sound of the cough of aneurysm. This, of course, is not essential to the diagnosis. The trachea was distinctly pushed over to the right. There was a large area of dulness over the chest extending from the junction of the first right interspace and the right parasternal line downward and outward to the left parasternal line, and spreading to the left anterior axillary line at the sixth interspace. By March, after *x*-ray treatment, the cough was very slight, the dyspnea was less, the tenderness and dizziness had almost disappeared. She was still sleeping poorly. There was still a slight receding pulse, the tracheal tug was still present, and the trachea still deviated to the right. There was also a distinct suprasternal pulsation, the cardiac dulness extended from the right parasternal to the left anterior axillary line, the systolic murmur at the base was still heard, an accentuated second sound was heard over the aorta and transmitted to the vessels of the neck. Sibson's[1] sign was not present. The lungs and abdomen were apparentaly normal. The blood-pressure was 172/90. The red blood-cells were 4,750,000. The white blood-cells were 10,600. The differential count: Polymorphonuclears, 83 per cent.; lymphocytes, 5 per

[1] Palpable diastolic shock at the aortic cartilage.

cent.; large mononuclears, 8 per cent.; transitionals, 2 per cent.; basophils, 2 per cent.

I did not see the patient again, but I was frequently in communication with her, and she continued the *x*-ray treatment until apparently restored to health. She is practically free of her rheumatism; has no cough; no more dyspnea than would be natural in a woman seventy years of age. She is cheerful and sleeps fairly well. Since the development of symptoms and the recognition of a mass in the superior mediastinum over three years have elapsed. It would be interesting to determine whether the tracheal tug and the deviation of the trachea have disappeared.

CASE II

The second case was first seen in December, 1922. Miss E. G. M., sixty years of age, a teacher by occupation, came to me complaining of spasmodic cough, first occurring at night; the attacks were extremely severe, and usually terminated when a small amount of mucus was expelled. She had dyspnea on exertion and frequent palpitation of the heart. Her climacteric had been normal and her life always extremely quiet. She had recently weighed 113 pounds, her highest. The symptoms had begun in September, 1922. Her weight was 109½ pounds. The pulse-rate was 112. The apex-beat was in the fifth interspace inside the midclavicular line. A powerful systolic shock and a faint diastolic shock and a distant systolic thrill were felt over the heart. The area of cardiac dulness extended from the midsternum to 2 cm. outside the left midclavicular line. A very strong tracheal tug could be felt, but there was no deviation of the trachea. A loud rough systolic murmur was heard over the entire heart, especially over the aortic cartilage. The second aortic sound was faint. A murmur and a faint sound were heard in the vessels of the neck. Occasionally a premature contraction occurred. Numerous sonorous râles were heard throughout the lungs. The vocal resonance was slightly louder over the right side of the chest. A vigorous systolic shock was felt in the epigastrium. There was also a loud systolic sound over the abdominal aorta and the femoral arteries. The blood was taken

for a Wassermann, which was negative. The blood-pressure was 180/78. Blood: Hemoglobin, 85 per cent.; the red blood-cells were 4,600,000; the white blood-cells were 8100. Specimens of the urine were normal.

Fig. 139.—Case II.

Dr. Pancoast reported: "The fluoroscopic examination showed very marked expansile pulsation of the arch of the aorta which gave the appearance of a slight dilatation, but the diagnosis of dilatation was not borne out by the plates. There was a large

shadow extending to the right of the heart very suggestive of a neoplasm. The left hilum was rather large in addition. The shadow observed on the right side was below the level of the third interspace anteriorly. The apices of the lungs were clear (Fig. 139). The pictures show that this tumor is located beneath the arch of the aorta. On a subsequent examination the physical signs remained practically the same. On the left side inspiration was interrupted synchronously with the action of the heart. The white blood-cells were 6000; the polymorphonuclears were 80 per cent.; the lymphocytes were 12 per cent.; the large mononuclears were 3 per cent.; the transitionals were 4 per cent.; the basophils were 1 per cent. The blood-pressure in the right arm was 170/90; in the left leg it was 182/120. The urine contained a trace of albumin and a trace of sugar. The electrocardiogram showed no preponderance, normal conduction, and an auricular extrasystole. Patient had had one series of *x*-ray treatment. Following this there had been nausea and she had vomited three times. She lost 4 pounds in weight, but the cough had been almost completely relieved. Dr. Pancoast reported after this that "there has been a slight diminution in the size of the mass, also a slight decrease in the density of the right side. I judge from this that there has been some improvement in the condition. The patient seems better."

Tumors of the superior mediastinum are of various kinds. They may be grouped as aneurysms; growths pertaining to the group of sarcomas; enlargement of the lymph-glands pertaining to the leukemias and pseudoleukemias; secondary carcinoma; dermoid cysts and infected lymph-glands.

In making the diagnosis of these conditions it is necessary first to recognize the existence of a mass in the superior mediastinum; second, to exclude aneurysm if possible; third, to determine the position, size, and nature of the mass if possible.

It is of no advantage to discuss in detail the symptoms of aneurysm; rather I shall discuss the symptoms of mediastinal growths, and many of these are common to both aneurysm and tumors.

The most important and constant is dyspnea occurring in

practically all mediastinal growths. It may reach the most extreme type. Ordinarily in the latest stages it is associated with slow, infrequent respirations. It is due principally to irritation and obstruction of the trachea by pressure.

Pain is very common. It is usually felt somewhere in the upper portion of the chest, often boring through to the back and to the region of the upper dorsal vertebræ. It may be worse at night. It may suggest pressure on some of the nerves, principally the brachial plexus, and shoot down the arm. It often requires an anodyne for its relief.

Cough is usually of the irritative character, almost continuous, with little expectoration, not as a rule "brassy," as is the cough of aneurysm, and there is no particular time of the day when it is worse.

Dysphagia is rarely present in the early stages of the tumor and may not occur at all. It is rarely so severe that regurgitation occurs. Rather it is a sense of pain or discomfort in the interior of the chest, felt during or after swallowing food.

Clinical manifestations which occur in the course of mediastinal tumors may be fever or emaciation, or both, depending upon the nature of the tumor. These may occur in sarcomas, in the leukemic tumors, in infected dermoid cysts, and in the infectious tumors of the lymph-glands.

Anemia is common, although in certain forms, particularly if there is much venous obstruction, polycythemia may occur.

Venous obstruction is one of the common manifestations, and may produce distention of the veins of the anterior portion of the thorax, the location of these distended veins depending upon the location of the tumor. It may obstruct some of the large trunks, giving rise to edema of an arm, or rarely there is obstruction of the descending vena cava, producing a picture similar to that caused by ruptures of an aneurysm of the arch into the descending cava, a picture that has been described particularly well by Osler, Pepper, and Fussell.

Pleural effusion may occur, usually characterized by the very rapid refilling of the pleural cavity. The fluid may be clear or bloody. Unless some complication has ensued, it is not pur-

ulent. Either side may be involved. Cases in which the thoracic duct has been obstructed, leading to chylous pleural exudate or ascites, have also been described, but they are rare.

The physical signs that have been described in association with mediastinal tumor are numerous. The combinations which occur are variable. As no one sees a large number of mediastinal tumors, his opinion as to the importance of various signs will be influenced by his personal experience. It is not possible, and probably not even desirable, to attempt to determine the relative importance of the various signs. Practically there is no sign which occurs constantly; there is nothing, therefore, that can be regarded as pathognomonic.

On inspection there may be seen difficult breathing; asymmetry of the chest or bulging of the chest wall; inequality of the expansion of the thorax; distention of the superficial veins, sometimes slight, sometimes extensive, as in the case described by Philips. Possibly there may be seen displacement of the larynx, limited movement of the larynx during the swallowing; edema of an arm, or of the head and both arms; slight exophthalmos, and in certain cases the attitude that denotes extreme dyspnea.

By palpation there may be determined the presence of an irregularity of the chest wall; unequal movements of the two sides of the chest; overfilled veins in the chest wall, friction, thrills, râles, and pulsation within the chest; restriction in the movement of the trachea during swallowing; tracheal tug; the size and movement of the thyroid gland; displacement of the trachea; the enlargement of the lymph-glands; enlargement or displacement of the spleen and the liver; inequality of the pulses.

By percussion may be determined the position of the various thoracic organs, the existance of abnormal areas of dulness, indicating the displacement of the heart, pleural effusions, abnormal masses within the chest; displacement or enlargement of the abdominal organs; the presence of the thymic sign, and particularly the areas of dulness over the upper part of the sternum, and the upper portion of the dorsal region of the spinal column; or hyperresonance, suggesting pressure or pneumothorax.

Auscultation furnishes much information. Over the lungs

may be heard stridulous breathing, râles of all kinds, but chiefly loud bronchial and cardiorespiratory murmurs, and interrupted breathing either during expiration or, particularly, during inspiration. Crepitation may be heard during respiration, particularly along the inner edges of the lungs during inspiration; breath sounds of all varieties, including harsh, bronchial, or amphoric breathing, increased vocal resonance, bronchophony or egophony (if there is an effusion), pectoriloquy, suggesting an effusion or a consolidation.

By auscultation of the heart there may be recognized variations in the intensity of the sounds, particularly the second pulmonic or aortic, variations in the transmissions of the sounds to the neck, down the borders of the sternum, or even to the epigastrium; the presence of murmurs, of which the most common is the systolic murmur, heard at the base of the heart and transmitted into the vessels of the neck; or thrills and murmurs may be heard in the neck by pressure; or the presence of Traube's or Durosiez's sign in femoral arteries. In addition, the splash and the coin test reveals a pneumothorax, and the second esophageal sound is lost when there is pressure upon the esophagus.

Practically, therefore, all methods of physical diagnosis are of value in the recognition of mediastinal tumor.

Of the clinical aids, the most important is the *x*-ray. But, if one may judge from Krause, on the recognition of mediastinal tumors by *x*-ray, this still is imperfect, and no very definite rules have been formulated. On the other hand, there can be no doubt of its extraordinary value. Of the laboratory tests, the same can be said as of the physical signs. The blood-pressure may show marked differences between the leg and the arm, without the existence of aortic insufficiency; changes in the blood may suggest the leukemic and pseudoleukemic types, or an infection; changes in the gastric contents may suggest a primary gastric carcinoma, which occasionally gives metastasis to the mediastinal glands. There are no characteristic changes in the urine. Sugar retention, after the ingestion of a glucose meal, is sometimes of value in the recognition of carcinoma, but too much dependence should not be placed upon it (Edward's test).

The similarity of these cases made it comparatively easy to diagnose the second case correctly. In the first case the diagnosis of superior mediastinal tumor was based upon the tracheal tug, the absence of signs of aneurysm, the persistent irritating cough, and the negative Wassermann reaction. With this information it seemed that there must be some non-syphilitic lesion producing an inflammatory but non-febrile reaction with adhesions, and this could only be some abnormal growth, therefore the patient was sent to the roentgenologist with a diagnosis of mediastinal tumor, perhaps more confidently than the evidence warranted. The important additional physical signs of deviation of the trachea and dyspnea on exertion should always arouse suspicion of some mediastinal condition, and lead to a search either for a definite evidence of aneurysm, or its exclusion.

The two cases recorded have in common the cough, the tracheal tug, the mild anemia, the differential blood-pressure, the positive *x*-ray findings, and the favorable response to *x*-ray treatment. It is noteworthy that both weighed more at the time of the first examination than they had ever weighed previously. These tumors do not cause cachexia. The nature of these tumors, of course, remains unknown. It is to be presumed that they belong to the class of lymphocarcinomas, since these are particularly amenable to *x*-ray treatment and respond to nothing else. A number of cases of this kind have been described, among the more recent of these, the cases of Philips, Cooley, Sorge, and Duncan (3 cases) may be mentioned.

Therefore, we can revise our prognosis of cases of this type from grave to favorable.

BIBLIOGRAPHY

T. B. Cooley: Jour. Amer. Med. Assoc., June 10, 1922, p. 1837.

R. Duncan: Medical Record, Abstract, Jour. Amer. Med. Assoc., August 6, 1921, p. 491.

Paul Krause: Groedel's Grundriss und Atlas der Roentgendiagnostik, Munchen, 1921.

McLester: Oxford Medicine, Vol. II.

John Philips: Jour. Amer. Med. Assoc., May 6, 1922, p. 1355.

Sorge: Abstract, Jour. Amer. Med. Assoc., August 26, 1922, p. 778.

CLINIC OF DR. T. GRIER MILLER

UNIVERSITY HOSPITAL

PERITONITIS CARCINOMATOSA COMPLICATING SCIRRHOUS CANCER OF THE STOMACH (LEATHER-BOTTLE STOMACH)

I WILL be unable to show you today a patient presenting the condition to which I wish to refer, but one has recently passed through our hands, and certain points about the case are so unusual and interesting that it would seem worth while to present an outline of our clinical and pathologic records of it and to discuss briefly some of the noteworthy features.

M. T., male, white, aged thirty-one, and unmarried, was admitted to the medical service of this hospital on August 2d. The records of the case may be summarized as follows:

Chief Complaints.—Pain in the epigastric region and vomiting.

History of Present Illness.—Having been in apparent good health previously, on May 11th, while very much overheated and sweating, he drank ice-water and then promptly developed a pain in the epigastrium, chilliness, and a cold sweat. He had to give up his work for the rest of the day. From then until his admission, almost three months later, he had a sense of oppression with burning in the epigastric area and gaseous and sour eructations at more or less regular intervals, these symptoms usually developing one-half hour or more after eating. They gradually increased in severity, and also a moderate diarrhea, consisting of two or three movements a day, came on. The oppression became real pain and it tended to radiate along the costal margins. The worst attacks usually occurred at about 2 o'clock each morning, and these were often relieved by vomiting or by taking a little soft food or hot water. All his symptoms

were aggravated by taking solid foods. His appetite had remained good, but he had been unable to eat because of the resultant pain, had lost some weight, and had grown quite weak.

Previous Medical History.—Negative as to illness, injury, operation, or venereal disease.

Family History.—Both parents were living and well at eighty years of age.

Social History.—Born in Poland, he had been in this country seven years, and during that time had worked for the DuPont Powder Co., wheeling materials used in the manufacture of high explosives, but not directly handling them. He used no tobacco or alcohol, and his living conditions were declared to be good.

Physical Examination.—He was of average physical development, fairly nourished, and his skin, especially that of the hands and face, had a slight icteroid tinge. Many of his teeth were crowned, there was some bridgework, and the general hygiene of the mouth was poor. Lungs were negative, as was also the heart, but for a soft systolic murmur at the base.

The abdomen had a normal contour, without any undue distention, tenderness, or rigidity. There were no masses or organs palpable and the peristaltic sounds seemed normal. No abnormalities of the nervous system were discovered. Rectal examination was negative.

Tentative Diagnosis.—Duodenal ulcer. (It should be explained that it is our custom to enter on our records a tentative diagnosis as soon as the history and physical examination are completed and before any laboratory reports have been received.)

Clinical Examinations.—(1) Blood: R. B. C., 4,450,000; W. B. C., 12,200; Hb., 80 per cent.; the white cells consisted of 90 per cent. neutrophils, 9 per cent. lymphocytes, and 1 per cent. large mononuclears. Subsequent white blood-cell counts within the first week were: 14,600 and 13,200, with neutrophil percentages of 89 and 82.

(2) Urine analysis negative.

(3) Gastric study: Thirty minutes after an Ewald meal only 4 c.c. of mucus could be recovered from the stomach through a small flexible gastric tube. Twenty minutes after another similar test-meal only 10 c.c. of slightly flocculent material were obtained. Tests on this showed no free hydrochloric acid and a total acidity of only 6. The occult blood test was positive, but otherwise the contents were entirely negative. When water was introduced into the stomach through the tube it could be withdrawn immediately, but on waiting three minutes none of it could be recovered. On inflation the stomach seemed to be in normal position.

(4) Phenolsulphonephthalein test (intravenous): First hour, 50 per cent., second hour, 15 per cent.; total, 65 per cent.

(5) Blood urea nitrogen: 15 mg. per 100 c.c. of blood.

(6) Blood Wassermann test negative.

(7) Feces examination negative.

(8) Gastro-intestinal roentgenologic study by Dr. H. K. Pancoast on August 4th: Under the fluoroscope the opaque material was seen to be expelled from the stomach almost as rapidly as it entered. Whether or not peristalsis was present could not be determined. The outline of the stomach could not be obtained and the duodenal cap was not seen. The colon was in good position, but showed a moderate amount of stasis. The plates gave no additional information.

A repetition of the stomach roentgenologic examination on August 16th, after the patient had been taking dilute hydrochloric acid in 20-minim doses with his meals, showed practically the same conditions, except that the plates indicated a cardiospasm, with slight dilatation of the lower end of the esophagus.

These various clinical examinations, therefore, showed only that he had a very rapidly emptying stomach (demonstrated by the stomach-tube and confirmed by the roentgenologic examination), and a moderate leukocytosis with a disproportionate increase in the polymorphonuclear elements. They did not establish a diagnosis. The increase in the gastric motility seemed consistent, however, with the tentative diagnosis of ulcer, though it was more marked than we would have expected, and

the leukocytosis suggested to some of us that such an ulcer might be nearing perforation. With this thought in mind and because of a loss of 10 pounds in weight and increasing epigastric discomfort, an exploratory laparotomy was advised on August 25th, but this the patient refused.

At about this time he began to take his food very slowly and soon showed some general improvement, but his leukocytosis increased (16,000, then 20,600, and 12,100). Another test-meal, with the patient on his left side and the foot of the bed elevated, gave results similar to the first one, only a little mucus being obtained. There was again no free hydrochloric acid.

On September 19th a considerable ascites was discovered with dulness to percussion over the epigastric region and extending down to the umbilicus, although no abdominal fluid had been demonstrated before. Later it was noted that this dull area varied in its position from time to time, single areas being alternately dull and tympanitic, and the leaves of the diaphragm were pushed up to the scapular angles posteriorly and to the fourth rib anteriorly on the right and to the fifth rib in the left anterior axillary line. These findings suggested for the first time that the patient might have a malignant lesion or lesions of the peritoneum, most probably colloid in nature.

Then (September 29th), as suddenly as it had developed, the abdominal distention began to subside, and just above the umbilicus a sense of resistance was made out on ballottement which suggested that a mass (about 6 x 2 cm.) might be attached to the anterior abdominal wall. With further subsidence of the fluid other smaller masses were demonstrable and crepitations were palpable (October 5th). By this time the patient had entirely lost his appetite and would swallow nothing but liquids. His leukocytes numbered 25,500, though the temperature continued normal most of the time, occasionally reaching $99\frac{1}{5}^{\circ}$ F. He was very weak and had a diarrhea. Examination of the chest suggested fluid in the left pleural sac and a puncture confirmed this. Only 20 c.c. were removed, this being yellowish and cloudy and containing a little blood. Later

vomiting set in, soon becoming fecal in character, and he grew steadily weaker, and died on October 16th. Two days before his death the leukocytes numbered 34,000.

Our final clinical diagnosis was carcinoma of the stomach, probably colloid, with involvement of the peritoneum. Fortunately an autopsy was secured, thus affording an opportunity to determine accurately the state of affairs. It was performed by Dr. Baldwin Lucke, and the following notes are abstracted from his very complete report:

Autopsy Report (abstract with special reference to abdominal findings).—Only a few cubic centimeters of somewhat turbid bloody fluid were present in the abdomen. The peritoneum was everywhere dull and covered with rather tough fibrinous exudate which had matted the intestinal coils together so that they formed a compact globular mass occupying the central portion of the abdomen. It was very difficult to separate the intestinal coils, and the attempt to do so generally resulted in tearing the walls. For this reason it was impossible to determine whether or not a perforation existed somewhere in the intestinal tract. On the right the diaphragm reached up to the fourth rib, and on the left to the fourth interspace. The stomach was almost hidden behind the costal margin and it was firmly adherent to the transverse colon, pancreas, and liver. Its remarkably small size at once attracted attention. The left pleural cavity contained 750 c.c. of turbid, slightly blood-tinged fluid.

At the junction of the esophagus and the stomach the gastric wall thickened abruptly, and throughout its entire extent showed an average width of 8 to 10 mm. The wall felt tough and had a grayish-white fibrous appearance. The serosa was covered with a tough exudate and occasional older fibrous tags. The mucosa was thick and thrown into coarse folds. Here and there superficial ulcerations were seen. The intestinal coils were so matted together that it was impossible to thoroughly examine them. The serosa was everywhere covered with a tough exudate, and when this was scraped off many serosal hemorrhages were seen.

Microscopic sections of the stomach showed the mucosa

largely necrotic. Throughout the mucosa and submucosa and the muscular layers were large cells with a deep-staining round nucleus, these having no particular arrangement. The submucosa was very fibrous and the muscular coats much thickened. Between the muscle-fibers of the latter there was also a large amount of cellular connective tissue. The serous coat was replaced by thick hyaline bands between which there were

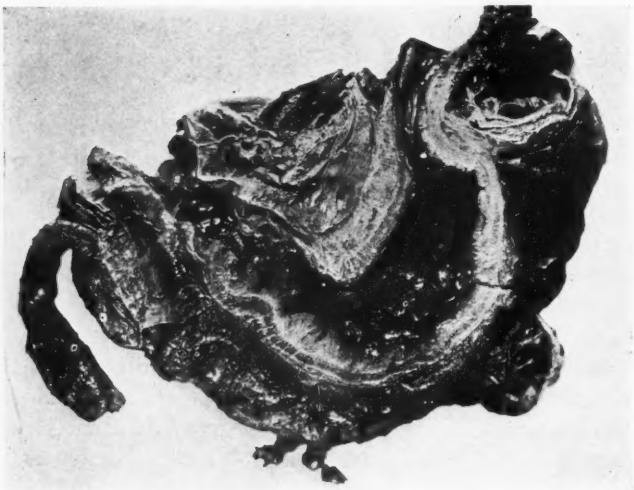

Fig. 140.—Specimen of stomach from described case of scirrhous cancer (leather-bottle stomach). Note the diffuse thickening of the stomach wall, the fibrous layer external to the muscularis showing especially well along the lesser curvature.

many of the foreign cells mentioned and great numbers of small round cells.

The mucosa of the small intestine appeared normal microscopically, but in the submucosa were many groups of large flat cells with prominent deep-staining nuclei and occasional mitotic figures (as in the stomach). The muscularis was infiltrated with nests of foreign cells, many of which were plainly undergoing mucoid degeneration. The serosa was as for the stomach.

Tumor cells of the type described were found also in widely dilated lymph-spaces of the pleural side of the diaphragm and in the much-thickened peritoneal side of the same organ. Similar cells were found in a lymph-gland removed from near the aorta and in the pancreas.

Culture of the heart blood was negative, but a few Gram-negative rods were discovered in smears from the peritoneal surface.

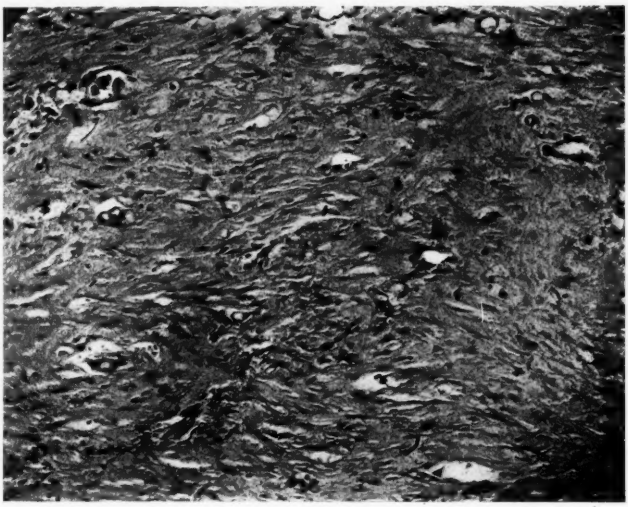

Fig. 141.—Microscopic section from outer portion of stomach wall, shown in Fig. 138. Note dense stroma containing scattered foreign cells.

On the basis of these findings the final pathologic diagnosis was diffuse scirrhous carcinoma of the stomach (leather-bottle stomach) with beginning mucoid degeneration and secondary involvement of the peritoneum, intestinal tract, diaphragm, lymph-glands, and pancreas.

COMMENT

Metastases of cancer of the stomach to the peritoneum are not at all uncommon, being exceeded in frequency only by such

secondary growths in the regional lymph-glands and in the liver. Martin, in Osler and McCrae's Modern Medicine, gives the distribution of metastases in 2156 cases of stomach cancer as follows: 44.1 per cent. in the lymph-glands, 33.2 per cent. in the liver, and 27.6 per cent. in the peritoneum and intestines. The medullary cancer and the adenocarcinoma, however, are the forms which most often and most readily give rise to such secondary involvements. Scirrhous gastric cancers are characteristically slow growing, spread slowly into the surrounding tissues, especially the muscle, and only rarely involve the peritoneum and intestines. Even when the scirrhous type does metastasize to the peritoneum, it usually gives rise to distinctly nodular lesions.

It is apparent, therefore, that our case is a most unusual one, in the first place, because the stomach cancer, being of the scirrhous type, spread to the peritoneum and intestines generally, and second, because of the character of the secondary involvement. The latter was not at all nodular, but rather was a diffuse infiltration of the walls of the intestine and of the peritoneum. It is also of great interest that the reaction in the peritoneum, as seen pathologically, indicated a true peritonitis.

Nichols[1], in discussing the rare forms of chronic peritonitis, spoke of a diffuse carcinomatous variety, and reported a case of the serofibrinous type which also had its origin in a scirrhous stomach cancer, and which showed diffuse malignant change in the peritoneum and omentum, with contraction of the mesentery. This case, however, differed from ours, in that there were innumerable nodules present. He said that the exact nature of the peritonitis which complicated carcinoma was obscure and intimated that it might depend on infection with organisms of low virulence. In his own case he suspected evidently that a secondary infection had occurred, but, in addition to this, he believed that the carcinosis itself led to marked proliferation of connective tissue.

There is the same uncertainty regarding the etiology of the peritonitis in our case. Occasional Gram-negative rods were

[1] Jour. Amer. Med. Assoc., 40, 696, 1903.

found in the smears from the peritoneal surface, but inasmuch as the autopsy was performed eighteen hours after death one cannot be sure that these were not secondary postmortem invaders. Against the assumption of infection by organisms are the lack of fever, the small number of bacteria found, and the absence of pus in the peritoneal cavity. That there was a true inflammatory reaction cannot be questioned in view of the microscopic evidence of newly formed fibrous tissue covering the muscular layers of the intestine and the presence in this of newly formed blood-vessels. Thus we can only say that our patient had an inflammatory reaction in the peritoneum and intestinal walls, a peritonitis, without asserting whether this was due to infection with organisms or due to the carcinomatous process, or to both. It is not believed that perforation occurred, because there were no acute symptoms or signs associated with the onset of the ascites, neither pain, tenderness, nor rigidity. While the presence of a leukocytosis might be used as an argument in favor of a septic peritonitis, it is to be remembered that a moderate leukocytosis is often associated with carcinoma of the stomach, more than 11,000 leukocytes being found in 31.2 per cent. of Taylor and Miller's[1] series of 182 cases, and in 11 of those cases, though this was not stated in our paper, the leukocytes numbered between 18,000 and 24,000. Furthermore, had there been a septic peritonitis the ready disappearance of the fluid would not have been likely, and finally, no certain rupture was found at necropsy.

We cannot be so sure, however, that perforation did not take place in another case which occurred in this hospital fifteen years ago, and which in many respects resembles this one. A man of sixty years, a weaver, was admitted with a complaint of epigastric pain which had been present for three months, and during that time he had lost 20 pounds in weight and had suffered from progressive weakness. On physical examination a movable irregular mass was found in the epigastric region. About two weeks after admission he became intolerant of food, developed a fever of 101° to 102$\frac{2}{5}$° F., much abdominal pain

[1] Amer. Jour. Med. Sci., 162, 862, 1921.

and tenderness, and a leukocytosis of 20,200. It was suspected that he had a rupture of his stomach, and he was transferred to the surgical service of Dr. Charles H. Frazier for exploration. No rupture was found, but after his death, two days later, an autopsy showed a large carcinoma of the stomach and a carcinomatosis of the peritoneum with peritonitis. Still no perforation was identified.

A condition more nearly analogous to that presented by our recent patient is described by F. Parkes Weber,[1] a condition in which "the surface of a serous membrane becomes diffusely infiltrated with carcinoma or sarcoma and in which there are inflammatory changes superadded, with small cell infiltration and diffuse formation of new thin-walled blood-vessels." He speaks of "peritonitis carcinomatosa" as the most common example, but points out that there do also occur "pleuritis carcinomatosa," "pachymeningitis carcinomatosa," "leptomeningitis carcinomatosa," and "leptomeningitis sarcomatosa." He reports a case of "pericarditis carcinomatosa" and also one of "peritonitis carcinomatosa," the latter occurring in a woman of forty-eight years, who had a short illness and ascites. At autopsy the peritoneal surfaces of the intestines, mesentery, and omentum were diffusely infiltrated with the carcinoma, and there was much inflammatory small cell infiltration. At one part of the parietal peritoneum there were very definite, newly formed blood-vessels visible to the naked eye. The outer walls of the intestines were thickened, hardened, and somewhat contracted, and the omentum and mesentery were also hardened and contracted. There was not a "leather-bottle stomach," but the primary carcinoma was at the neck of the gall-bladder in this case.

Three cases of "leather-bottle stomach" with diffuse carcinomatosis of the whole intestinal tract have been reported by Nuttall and Emanuel,[2] but in only 2 of these was there an associated peritonitis, and 1 of these was of the septic type and clearly due to a cecal perforation. The other resembled

[1] Practitioner, 100, 246, 1918.
[2] The Lancet, 1, 159, 1903.

our case in that there was ascites and an acutely inflamed peritoneum covered with a fibrinous exudate matting the intestinal coils loosely together and easily peeling off the intensely injected surface beneath. In the third case there was no peritonitis. Metastases to other organs occurred in but one of their cases, and that was to the gall-bladder and to the kidney.

A microscopic study of specimens from these cases showed that the original lesion occurred in the wall of the stomach, and that in the small intestine and colon the infiltration was mainly in the submucous and subserous layers, the two being connected by strands of growth. Colloid degeneration had occurred, again as in our case, but this was determined only by the microscope, there being no gross evidence of this change. It was especially marked in the outer layers of the bowel wall.

These cases, while resembling ours in the main, differed in that the metastatic process in the intestine seemed older, the bowel wall being much thickened and indurated. Furthermore, the involvement was not so perfectly uniform, being distinctly patchy below the stomach. In one case at least the peritoneum itself did not seem to be particularly affected, though in all, as in ours, the submucous and subserous layers were most markedly the seat of the malignant process.

Speculation as to the method by which the secondary peritoneal and intestinal involvement is brought about in all of these cases is interesting. It is usually assumed that metastases occur by the blood-stream (as in liver and lung involvements), by the lymph-stream (as in glandular involvement), or by direct extension. The first method, by blood-stream, would not seem a logical explanation, since the venous blood from the stomach goes directly to the liver by the gastric and portal veins and does not flow toward the general peritoneum. Lymphatic extension might at first thought seem more likely, but in such an instance it would be expected that the neighboring lymph-glands would be first and most markedly affected, and this does not seem to have been true. If the metastasis should occur by direct extension it would seem reasonable to expect that neighboring organs would be primarily involved, and not

that there would be, so quickly at least, a generalized peritoneal invasion. Thus none of these methods seems to explain the situation satisfactorily, and another method, a theoretic one, it is true, has occurred to us: a sudden spilling of cancer cells into the peritoneal cavity. It has long been believed that this is the method by which rectal metastatic lesions develop from stomach and other upper abdominal cancers. Furthermore, in 1893, Allen J. Smith,[1] in discussing generalization of cancer of the stomach and in reporting a case with both pleural and peritoneal diffuse metastases, suggested this idea, believing that minute particles getting free in the general cavity were scattered mechanically by the intestinal movements. While usually such particles, becoming attached at various places, have been assumed to set up local reactive inflammations of a malignant nature, so giving rise to nodules, it requires no great stretch of the imagination to think of these minute lesions spreading rapidly along the peritoneal surface by direct extension and by lymphatics, and so giving rise to a diffuse infiltrative process. Particularly does this seem reasonable when the cancer is of the scirrhous type which characteristically spreads in this way. Such a spilling might result from minute ruptures of the gastric peritoneum, particularly when the cells were degenerating, as indicated by colloid change.

Such a method of spread of the cancer cells might also explain the rather sudden development of the ascites in our case, and likewise its equally quick disappearance. Assuming the possibility of a liberation of considerable numbers of these cells at one time a general irritation of the peritoneum would take place, manifested first by a profuse serous exudation. Such an exudation might at first be too great for the ordinary channels to carry it off, but later, as the fibrinous element in it should become more marked and the serous less profuse, the ascites would disappear. The general pathologic principles underlying inflammation would seem to justify such an assumption, and the presence of the markedly fibrinous exudate with adhesions found at autopsy would also lend support. Further-

[1] Trans. Texas State Med. Assoc., May, 1893, p. 166.

more, such changes as were found in the intestinal walls at autopsy in our patient might readily have developed within the four weeks that intervened between the development of the ascites and death.

One other point about this case, and one having a bearing on diagnosis, is deserving of comment. It has to do with the rapid emptying of the stomach as demonstrated by the gastric tube and by the Roentgen ray. Although at first interpreted as consistent with a diagnosis of duodenal ulcer, it is now recognized that this was a hasty and ill-considered opinion. It should have been remembered that in duodenal ulcer, in spite of the early rapid gastric evacuation, there is almost always some delay in the discharge of the last portion of the meal, and also that even the initial hypermotility is rarely if ever so marked as it was in this case. Such roentgenologic findings have previously been described in cases of marked thickening and rigidity of the stomach wall, as in a case of linitis gastrica reported by Sailer,[1] and similar rapid passage of an opaque mixture through a fibrosed colon has been observed by Lawrason Brown and others in cases of hyperplastic tuberculosis of the cecal region. Consequently, when such a rapid passage of the opaque substance through the stomach was observed fluoroscopically in our patient, it should have suggested at once a rigid gastric tube through which the mixture was flowing or being squirted, and one that was incapable of ordinary peristaltic movements. Such a realization would probably have led us at that time to a correct diagnosis of the gastric lesion.

This suggestion in diagnosis and the unusual picture, disclosed at autopsy, of a diffuse secondary carcinomatous infiltration of the peritoneum without nodularity and with microscopic evidence of peritonitis are the reasons that have impelled me to present this case of leather-bottle stomach.

[1] Amer. Jour. Med. Sci., 151, 321, 1916.

CLINIC OF DR. O. H. PERRY PEPPER

UNIVERSITY OF PENNSYLVANIA

CLINICS TO A FIRST-YEAR CLASS IN MEDICINE

ONCE a week throughout the year the First-year Class in Medicine at the University of Pennsylvania receives a clinical lecture in the amphitheater of the University Hospital at which one or more patients from the wards of the Medical Division are demonstrated.

In these hours the subjects presented are correlated as closely as possible with the topics being covered in the courses of anatomy, physiologic chemistry, and, later, of physiology. It is the object of these hours to illustrate to the students that the fundamental branches which they are studying have practical applications in medicine, and are daily employed in the diagnosis and treatment of disease. At the same time a certain amount of medical terminology is acquired, and the students also receive a preliminary introduction to the sick person and to disease.

It is hoped in this way to stimulate the student's interest in an intelligent study of the fundamental branches and to make it clear to the student from the very start that everything which he is studying is actually fitting him to practice medicine. The purposes of this course of clinics are with limitations identical with the suggestions made by President Henry S. Pritchett in the 1921 Report of the Carnegie Foundation, and are in line also with the suggestions for a revision of the undergraduate curriculum prepared by Dr. Ray Lyman Wilbur.[1]

The following brief abstracts of sample clinics have been selected from those presented during the present (1922–23)

[1] Jour. Amer. Med. Assoc., May 27, 1922, 78, p. 1630.

course, and are printed here simply for such teaching interest as they may possess.

I. DIABETES MELLITUS WITH SLIGHT ACIDOSIS. A DISCUSSION OF THE BUFFERS OF THE BLOOD

In your lectures this week in Physiological Chemistry you have heard discussed the nature of buffer action, and you have learned that buffers are substances which by their presence in solution increase the amount of acid or alkali that must be added to cause a unit change in the hydrogen-ion concentration. You have also been told that buffer systems are present in the blood, and these buffers have been detailed to you and their action explained.

The patient whom I will now present to you has a disease in which these buffers of the blood may be called upon to their utmost to maintain the constancy of the reaction of the blood, and so to protect the body from the serious or even fatal effects which result from any but a trifling shift in the reaction. This disease is diabetes mellitus.

In this disease, according to the present views, the fundamental fault is a deficiency of the so-called internal secretion which the pancreas gives off into the circulating blood. It is from certain groups of cells called the islands of Langerhans that this secretion is given off, and it is entirely separate and distinct from the other or external secretion of the pancreas which is passed off into the intestine. The internal secretion of the pancreas is essential for the proper combustion of carbohydrate, and in its absence or marked decrease a disturbance of carbohydrate metabolism occurs which has important and far-reaching results.

In the first place the body fails to burn all or part of the carbohydrate foods eaten, and so loses the value of this food. The unburned sugar accumulates in the blood and after the concentration has reached a certain level the sugar escapes in the urine. The presence of sugar in the urine thus constitutes one of the important signs of diabetes mellitus. Associated with the high level of blood-sugar there occurs a marked thirst and a

great increase in the amount of urine. It was almost eighteen hundred years ago that the thirst and increased urine led to this disease being named "diabetes," from the Greek word meaning a syphon, while the sweetness of the urine which led to the term "mellitus" being added was not recognized until the fifteenth century.

In the second place, the sufferer with this disease finds it difficult to obtain sufficient nourishment. The more starchy food and sugar that is eaten, the more is lost in the urine and, unfortunately, this is not his only trouble, for as a result of the failure of carbohydrate combustion a disturbance of fat catabolism occurs. Apparently sugar must be burned for fat to be completely burned, and since in the diabetic the sugar is not burned, neither is the fat properly catabolized. As a result of this failure to burn carbohydrate and fat the body is insufficiently nourished, the patient, in spite of being hungry and eating enormously, consumes his own tissues and marked loss of weight occurs.

We have now mentioned the cardinal symptoms of this disease—loss of weight, hunger, thirst, increased urine, and the presence of sugar in the urine. These are the symptoms which our patient complains of. Let us review his story.

L. H. B. is a college graduate and has been a metallurgic engineer. He has worked very hard all summer and has lost 20 to 25 pounds in weight, which he attributed to his overwork. In an effort to improve his weight he commenced eating more and more starchy food, but continued to lose weight. Three weeks before admission to the hospital he first noticed an excessive thirst with a dryness and burning in his mouth. Soon afterward he noticed that the amount of urine was greatly increased and that he had to arise several times at night to void. Sugar was found in the urine by a doctor to whom he went five days before admission and the patient was at once sent to the hospital.

You will appreciate at once that the cardinal symptoms which I have detailed to you are all present in this patient's story. It is pathetic to hear him tell of his attempting to prevent

the loss of weight by eating more freely of starchy foods, while we know that it was not only futile, but harmful.

As you look at the patient you see at once that he is underweight, but his color is good, which would be surprising except that we know this to be a characteristic of this disease. In all other respects the physical examination is negative except that as I examine the tongue and throat I am aware of a distinct sweetish, fruity odor to his breath.

Now let me place on the blackboard a few of the results of laboratory tests which have been performed in the study of this patient's condition, and for contrast the normal figures will be added.

Urine for twenty-four hours after admission:

	Sugar.	Total ketones.	Ammonia N.
Normal	0	Mere trace	0.5 gram
Patient	38 grams	1.1 gram	3.82 grams

Blood on day following admission:

	Sugar, per cent.	Ketones, per liter.	Plasma $NaHCO_3$ content in terms of CO_2 volumes per cent.
Normal	0.080–0.120	0.013	55–60
Patient	0.177	0.468	37

Certain differences from the normal are obvious to you at a glance: there is sugar in the urine and too much sugar in the blood; there is a definite increase of ketones in the urine and in the blood; an increase of ammonia in the urine, and a decrease of CO_2 in the blood. The changes in the sugar have already been discussed, but what are these ketones and why are they increased in the blood and urine of this patient?

A few minutes ago we were discussing the fact that if carbohydrates are not burned in the body there results a failure of the proper combustion of fats. This disturbance of fat catabolism brings it about that instead of the fat being broken down to its normal end-products, its catabolism is arrested and a large part of it is to be found in the form of beta-oxybutyric acid, aceto-acetic acid, and acetone. These substances are the so-called ketones and the former two are acids. It is these

substances which give to the breath the fruity odor which I have mentioned.

In an indirect way, therefore, we have here another measure of the failure of the body to burn sugar, but we are more interested in the amount of ketones in the blood and urine for another reason. Two of these ketones are acids, and the introduction of these acids into the blood at once threatens to change the reaction of the blood. This the body cannot stand, for it is a threat at life itself, and a number of mechanisms are set into motion to prevent its accomplishment. For example, the process by which urea results from the metabolism of protein is partially halted at the ammonia stage, and this alkaline substance helps to maintain the normal reaction of the blood. We measure the amount of ammonia in the urine to give us information as to the severity of the threat by the ketonic acids.

And now we get back to our starting-point: in the blood, as we have said, there are buffers. Will you name for us one of the constituents of the blood which has a buffer action?

STUDENT: The bicarbonates.

DR. PEPPER: Yes. What others?

STUDENT: The phosphates and the proteins.

DR. PEPPER: Yes, the bicarbonates, the phosphates, and the alkali salts of the proteins all act in this capacity. All are salts of weak acids and may be thought of simply as reservoirs of alkali. In addition to this the sodium bicarbonate acts to neutralize any foreign acids which enter the blood; the foreign acid combines with the sodium bicarbonate to form the sodium salt of the acid and carbonic acid. The excess of the latter is then blown off through the lungs. The lowering of the amount of $NaHCO_3$ is, therefore, an index of the amount of foreign acid which has been neutralized.

What other substance in the blood did Professor Wilson tell you acts to maintain the blood pH near its physiologic point?

STUDENT: The hemoglobin.

DR. PEPPER: How does hemoglobin act in this capacity?

STUDENT: The reduced form of hemoglobin is a much weaker acid than the oxidized form.

DR. PEPPER: That is correct. In venous blood a greater part of the hemoglobin is in the reduced state, and so base is liberated and neutralizes the carbonic acid which is taken up from the tissues. As the blood passes through the lungs the CO_2 is given off and the hemoglobin shifts to the oxidized form. In this way the reaction of the blood is kept constant despite the difference between the carbonic acid content of the arterial and venous blood.

The distribution of these buffers in the blood-plasma and in the blood-cells is of great importance, but cannot be discussed here. It is worth remembering, however, that the phosphates and the hemoglobin are in the cells, while the bicarbonate and protein are present in both cells and plasma.

Clinically in a patient with diabetes mellitus we are anxious to know to what extent the ketonic acids have encroached on the ability of the buffers of the blood to maintain the blood pH at its usual level. In the present instance we have already obtained some information from the amount of ketones in the blood and from the amount of ammonia in the urine, but we have still other methods. The pH of the blood may be determined directly by the simple colorimetric method of Cullen, or we may indirectly find out by measuring the concentration of the CO_2 in the venous blood. This tells us how much base is left to combine with the weak carbonic acid after the stronger ketonic acids have been neutralized.

The normal figure for the CO_2 content of blood-plasma is about 60 to 70 volumes per cent. The blood-plasma of our patient contained, however, on admission to the hospital only 37 volumes per cent. This is a moderately severe reduction and taken in conjunction with the other information which we have justifies us in concluding that our patient had at the time of admission not only diabetes mellitus with hyperglycemia and glycosuria, and ketonemia and ketonuria but also a reduction in the alkali reserve of the blood. In other terms, there was an "acidosis" present, of a degree sufficient not to be entirely neutralized by the buffers of the blood.

You see, therefore, that in the clinical study of this patient

we make extensive use of the principles, facts, and methods of physiologic chemistry, and that we employ in our diagnosis and as an aid in our treatment the very knowledge concerning the buffers of the blood which you have recently been receiving in the course in that subject.

Since admission this patient has rapidly improved. We have administered to him the new preparation of the internal secretion of the pancreas recently prepared by certain Toronto investigators. This enables him to burn sugar. Within a very few days the sugar disappeared from the urine, the blood-sugar fell to a normal level, the ketones almost disappeared from the urine, and the plasma $NaHCO_3$ content rose to normal. Today his diet contains about 75 grams of protein, 125 grams of fat, and 70 grams of carbohydrate having a value of about 1700 calories. He feels well and is holding his weight. No pancreatic extract has been given him for a week and no return of his former condition has as yet been observed. The blood-sugar recently was 0.122 per cent., the plasma CO_2, 58 volumes per cent. These are normal figures. This is good evidence that he is now burning enough sugar, thanks to his own pancreatic activity, to keep his blood-sugar at the normal concentration, and to prevent the accumulation of ketones and thus prevent any impairment of the alkali reserve. The buffers are once more normally at work maintaining the usual pH of the blood. In fact, on today's figures alone it would be impossible to diagnose the presence of diabetes mellitus or of any disturbance of the acid base equilibrium of the body.

II. SEPTIC MENINGITIS SECONDARY TO OTITIS MEDIA

For the past few days your class has been receiving instruction concerning the anatomy of the skull in your course in osteology, and I have, therefore, selected for today's clinic a subject which illustrates the practical importance of the information which you are acquiring. The patient whose illness will serve as our text unfortunately died yesterday, but the postmortem examination findings which I will describe to you add to the value of the case from a teaching point of view.

A. T., a male twenty-one years of age, was taken sick on October 1st, a little over two weeks ago. His first symptom was a sudden chill, and nothing further developed for three days. On October 4th he had another chill and headaches appeared and continued. Further chills occurred on October 6th and 7th, and on the 9th the patient was admitted to this hospital still complaining only of headache and chills. The chills had been severe, and like most true chills had commenced with a feeling of coldness which increased until the patient shook violently with cold and the teeth chattered. This cold period lasted for about a half-hour and was followed by fever, thirst, and profuse sweating. This is the usual sequence of events in a typical chill such as occurs so commonly in malaria and at the onset of certain infectious diseases, as, for example, pneumonia.

The patient's headache was chiefly in the back of the head and he described it as being of a "jumping" type. The only other item of history which the patient gave was that he believed he had lost 12 pounds in the past three weeks. He had never been seriously ill before except for "pneumonia" in 1918.

Because of his story of repeated chills the possibility of malaria evidently occurred to the historian, and we are told that in July the patient went to Texas as an ordinary seaman and later to Virginia, but he does not remember being bitten by mosquitoes.

In the examination made on admission to the ward it is noted that the patient looked ill and was restless. The tongue was coated, the breath heavy, the lips dry and parched, all of which are simply signs of fever. The tonsils were ragged and showed evidences of being infected; "several pus points" were seen on them. The ear drums were normal in appearance. No abnormal findings were noted in the chest, but in the abdominal examination it was observed that the spleen, which normally is not palpable, was easily felt and seemed enlarged. The patient was not delirious, was conscious, and no evidence of disease of the nervous system was noted.

There was fever, the temperature being $103\frac{2}{5}^{\circ}$ F., which is

5 degrees above normal. The pulse-rate was 106 per minute. The respirations were 24 per minute.

The only laboratory examination which needs to be mentioned at this time is the count of the so-called leukocytes of the blood, which form one of the body's defences against infection, and which increase greatly in number in the blood in the presence of many, but not all infections. The pus which you are familiar with, for example, in boils is formed of these leukocytes. Normally the number per cubic millimeter of blood is from 6 to 8000; in the blood of the patient whom we are discussing the count was 15,400, not a very great increase, but distinctly abnormal.

To summarize the evidence thus far obtained: A young man previously healthy except for some loss of weight is taken acutely sick with chills and fever, later he develops headache. Eight days later he enters the hospital and examination reveals fever, tonsillitis, an enlarged spleen, and an increase in the leukocyte count.

All of this evidence pointed to an infection, and the problem in diagnosis is concerned with determining the nature of this infection—what infection? where located? The tonsillitis alone did not seem adequate to explain the severity of the symptoms. Headache is a common symptom in any fever. Repeated chills, however, occur characteristically in only certain infections, and an enlarged spleen also is especially evident in certain infectious diseases. Both are the rule in malaria, but in this disease it is not usual for the leukocyte count to be increased.

However, we examined the patient's blood repeatedly and carefully for the protozoal organism, which is the cause of malaria and which is discoverable in the vast majority of instances, on or in the red blood-corpuscles of the patient. In this case, however, none was found.

The reasons for ruling out typhoid fever, pneumonia, etc., need not be given here, but it will suffice to say that after four days, during which the patient's condition had shown no change and during which further chills had occurred, we had arrived at no diagnosis. The temperature chart shows the fever during

this period; there was no increase of the pulse or respiratory rate beyond that incident to the fever.

On October 12th it was noted that the patient seemed mentally slow, and on the 13th there developed rigidity of the neck and pain in the back of the head. The next day these signs had greatly increased, the patient had become stuporous, and the stiffness of the neck had extended down, involving the muscles of the back. He became completely unconscious during the day of the 14th and died during that night.

The developments appearing on the 12th and 13th of the month made the diagnosis obvious. The patient had a meningitis, an inflammation of the meninges, the thin coverings of the brain, and this we were able to demonstrate by inserting a hollow needle into the canal of the spinal column and removing a few cubic centimeters of the so-called cerebrospinal fluid. This fluid circulates through the fluid-containing spaces in the brain, between the brain and its coverings, and down along the spinal cord between the cord and its coverings which are continuations of the meninges of the brain. This fluid normally is water-clear and contains only a few leukocytes; in this instance it was cloudy from an enormous number of these white cells of the blood, a sure evidence of the presence of infection.

Having arrived at the diagnosis of a meningitis our problem was only half-solved. We were not able to find in the cerebrospinal fluid the specific bacteria which would have justified a diagnosis of tuberculous meningitis or of the so-called epidemic "cerebrospinal" meningitis of which you have, I am sure, heard. It was obvious very promptly that this meningitis was not of either of the above special types, but was due to some one of the bacteria which are constantly about us, ready to cause trouble and local infection if they can pass the outer defences of the body. Let us call this, then, an instance of septic meningitis.

We then had to ask ourselves the question, how did the bacteria reach the meninges in this instance, and how did they penetrate within our patient's skull to commence the infectious process which led to his death?

No wound occurred through which the bacterium might have entered and no fracture of the skull.

Was there any evidence of disease elsewhere in the body from which the infection might have been transmitted in some way to the brain coverings?

STUDENT: The tonsillitis.

DR. PEPPER: Quite right. Bacteria are carried from one part of the body to another by the blood-stream, the lymph channels, or they pass along some anatomic structure such as the digestive tube or the urinary passages. It is not likely that infection would pass from the tonsils to the brain by the blood- or lymph-stream, the other pathway requires more consideration. Do you know any open connection between the naso-pharynx and the interior of the skull?

STUDENT: No, but the eustachian tube connects the naso-pharynx with the middle ear.

DR. PEPPER: Yes, and once infection reaches the middle ear it has taken a long step on its way to the brain. The eustachian tube opens into the tympanic cavity and this space continues backward into the mastoid air cells, so that infection once started along the eustachian tube may extend throughout this whole tract. From the tympanic cavity infection may spread upward through the thin roof of the tympanum and produce an abscess immediately outside the coverings of the brain which at this point are fused to form a single layer. This latter fact explains why extension of infection along this route fails to lead to a wide-spread meningitis between the layers of the meninges, but rather extends directly into the brain substance and forms an abscess in the temporal lobe.

On the other hand, a number of small veins pass from the tympanum and reach the lateral sinus by way of the jugular bulb; others reach another of the venous sinuses. The lateral sinus is one of a number of large thin-walled blood spaces which collect the venous blood on its way back to the heart. Along these veins the infection may be carried on into the interior of the skull. There are still other routes from the tympanic cavity by which infection may spread, but these examples will

suffice, and from the mastoid air cells the infection may also extend directly to the lateral sinus which grooves the inner aspect of the skull immediately over them. Sometimes the infection spreads outward and does not reach the brain or its coverings, and these patients are in much less danger. When, however, the infection has reached the brain, the brain coverings, or the large venous sinuses, then the danger is great. Infectious meningitis is a very serious disease and so is brain abscess.

When the lateral sinus is affected the infection forms a sort of clot in the vessel which may even completely fill the vessel; from this clot the infection reaches the general blood-stream and is carried all over the body. Or the infection may pass from the sinus to the base of the brain and there lead to a meningitis.

Now as I hold this opened skull before you what is this ridge of bone to which I point?

STUDENT: Mastoid portion of the temporal bone.

DR. PEPPER: In this groove lies the lateral sinus very close to the mastoid cells which are covered only by a thin layer of bone at this point. It was at this point that the postmortem examination revealed the source of our patient's meningitis. The bone of the mastoid region here was soft and diseased, and on opening into the mastoid cells pus gushed out. The lateral sinus was filled with clot and at the base of the brain also there was some pus and the meninges were inflamed and thickened.

In retrospect the whole picture becomes clear. The patient developed a tonsillitis; the infection spread up the eustachian tube to the middle ear, thence to the mastoid air cells. The bony wall of these air spaces became diseased and the infection extended directly to the lateral sinus. The chills were evidences of the extension of the infection to the general blood-stream, and the final development of meningitis was due to the extension of the infection to the base of the brain.

It is somewhat unusual that no localizing symptoms were present to direct our attention to the ear, but this does happen occasionally. That the ear drums were normal in appearance should not have misled us, as this may often be the case. Finally

it is interesting to note that cultures of the same bacteria were obtained during life from the tonsils, blood-stream, and spinal fluid, and after death from the pus in the mastoid air cells.

That this sequence of events is commoner in children is due to the thinner bones of the skull. That meningitis more frequently follows right-sided mastoid disease than left sided is again due to the thinner bony wall over the mastoid cells which, in turn, is explained by the fact that the wall is encroached upon by the larger right-sided lateral sinus.

It seems unnecessary to emphasize the moral which this patient's story points. An understanding of this case is entirely dependent upon a knowledge of the anatomy of the skull. Once we learn that there is a route by which a nasopharyngeal infection may spread to the middle ear and many routes by which infection may from there reach the interior of the skull, then we know why middle-ear disease is the commonest cause of septic meningitis.

CLINIC OF DR. JOHN H. MUSSER, JR.

GRADUATE SCHOOL OF MEDICINE, UNIVERSITY OF PENNSYLVANIA

UNUSUAL TYPES OF LEUKEMIA

BEFORE discussing the 2 cases I wish to present to you today I want to report briefly on the 2 patients that I showed you last year. The one patient has been under observation for three years with a severe leukemia, during which time she has had more or less persistent Roentgen-ray treatment. For the past year her leukocyte count has only once risen above 30,000. The percentage of lymphocytes has remained about 6 per cent. She has, however, an extremely pronounced anemia, with red cells under 2,500,000 and hemoglobin under 50 per cent. This I interpret as a well-marked evidence of bone-marrow failure. She had developed severe cystitis and pyelitis and her general condition is extremely poor.

The second patient is the man with acromegaly associated with leukemia. His condition is apparently unchanged. In the past year, when his leukocyte count went up to about 35,000, he has had one course of Roentgen-ray treatment. During the rest of the time his count has remained between 10,000 and 16,000; the hemoglobin and red cells have remained about normal. His general condition is very good.

The 2 cases I am going to show you today will not be seen in the flesh, but rather in their preserved specimens, as autopsies have been performed on both these cases.

CASE I

J. S. White, male, aged sixty-five, admitted to the Philadelphia General Hospital May 6, 1922.

Chief Complaint.—Weakness, loss of weight, vomiting, pain in the abdomen.

Present Illness.—Began in December, 1921, when patient noticed he began to tire easily. He felt weak and could no longer do the amount of work which he was accustomed to do. Weakness progressed so that in a few weeks he had to stop work entirely.

Shortly after this, about a month before entering the hospital, he complained of abdominal pain, dull, aching in character, located around the umbilicus. The pain was increased by taking food, particularly solid food. He vomited occasionally one-half to two hours after eating large quantities of heavy foods. The pain and vomiting have become gradually more severe, and with the increase in the severity of the symptoms he has been forced to eliminate the more solid foods from his diet, until at the present time he is taking only liquids, and the majority of these are vomited within one to three hours after ingestion. The vomitus is greenish in color and has had no blood. Feces are apparently normal. He belches considerable gas and is constipated.

The patient has a slight unproductive cough, but no hemoptysis and no night-sweats.

There is no edema and no precordial pain.

Nocturia twice. Some difficulty in starting urinary flow. No headaches. Some vertigo. The patient has lost 30 pounds since onset of trouble.

Past Medical History.—Yellow fever in 1912; in Mexico at the time. Occasional cramp-like pain in right leg. Otherwise healthy.

Venereal.—Gonorrhea many years ago, but has never had lues.

Habits.—Considerable alcohol, but says he was never intoxicated. He has always used tobacco and coffee to excess.

Social.—Mechanical engineer. Good living conditions. Single.

Family.—Several members of the family, including his mother, died of cancer. No other familial tendencies.

Physical Examination.—Patient is a white male about

sixty-five years of age. Well developed and fairly well nourished. Moderate signs of senility. Seems to be in a weakened condition, but co-operates well.

Skin and Mucous Membranes.—Abnormal pigmentation of face, hands, and thighs near the scrotum. Some senile changes. No jaundice. No eruption.

Glandular.—Right epitrochlear and inguinal glands are palpable.

Head.—Grossly normal. Skin deeply pigmented.

Eyes.—Some puffiness about the eyes. Right pupil is slightly irregular. Beginning cataract in left eye.

Ears.—No discharge. Function impaired.

Nose.—Grossly normal.

Mouth.—Teeth show pyorrhea and dental caries. Tongue is heavily coated. Pharynx is normal for age.

Neck.—No adenopathy. No abnormal pulsations.

Thorax: Pulmonary.—Expansion fair and equal. Palpation is normal. Percussion note is resonant throughout. Breathing is bronchovesicular in type. No râles. Fremitus and resonance are normal.

Cardiovascular.—Apex in fifth interspace 13 cm. to left of midsternal line. No thrills. Rate and rhythm are normal. Sounds are distant and somewhat weak. Valve sounds clear. No murmurs. Radials are slightly sclerosed, equal, and synchronous. Blood-pressure 155/90.

Abdomen.—Wall of good muscle tone. Liver edge palpable on deep inspiration. No dulness, no masses, no rigidity, Slight epigastric tenderness associated with considerable pain.

Extremities.—Grossly normal.

Neurologic.—Reflexes normal. No Babinski. No clonus. Normal co-ordination. Slight tremor of fingers.

A blood-count was made as soon as the patient entered the hospital, and it showed a total number of white cells of 102,300, of which 22 per cent. were polymorphonuclears and 78 per cent. were diagnosed as lymphocytes.

The urine on admission showed a specific gravity of 1024, trace of albumin, many hyaline casts, many leukocytes.

The blood urea nitrogen was 23 mgm. per 100 c.c.

Blood Wassermann was negative in all antigens.

Two days after admission the white count had risen to 126,200, 13 per cent. being polymorphonuclears and 87 per cent. lymphocytes. The lymphocytes could not be definitely classified either into the large or small variety, nor was there any granulation in the protoplasm, nor were the cells myelocytic. It was quite apparent they were young, immature form of white cells which might more properly be classified lymphoblasts or myeloblasts.

On account of the persistent vomiting, which was treated without avail by medical measures, it was decided the patient should be operated upon. He was transferred to the Surgical Service. The Roentgen ray confirmed the clinical diagnosis. The roentgenogram showed pyloric obstruction probably due to malignancy. He was operated on May 15th and died the following day.

Clinical Summary.—This patient presented the signs of an acute gastric obstruction. At operation this was confirmed, as there was a partial obstruction due to extensive mass of adhesions. One of the most interesting findings was an abscess in the lesser peritoneal cavity, the cause of which we were unable to determine at the time of the operation. Associated with this was a marked leukemic reaction, which was unusual. There was no clinical evidence whatsoever of a disordered blood-picture. Spleen, liver, and superficial lymph-glands were not enlarged, nor did the man have the facies, the oral condition, and so on, of leukemia.

At autopsy the following report, in brief, is presented for your consideration:

White male, sixty-five years old, 165 cm., weighing 125 pounds. Normal framework. Skin is free from jaundice and edema. Scleræ are clear. Orifices and genitalia negative. Recent surgical wound of the abdomen, with rubber tube and gauze drainage. The heart, lungs, and thorax are essentially negative. The abdomen shows intestinal coils matted together by scanty, fibrous adhesions. Gauze drain passes through the

greater omentum into the lesser peritoneal cavity, where a mass of necrotic material is found. The spleen weighs 150 grams, is normal in consistency, capsule is unthickened. Cut surface is dark red. The liver weighs 1350 grams and is normal in consistency. Lower border is sharp. Capsule unthickened. Cut surface shows normal texture. Sections from the various organs show no evidence of leukemia. Spleen shows some congestion, liver shows cloudy swelling and biliary pigmentation.

Discussion.—This case presents an unusual type of bone-marrow reaction. I hardly think it is fair to say that it is a true leukemia, due to the fact that there was no evidence of leukemia postmortem. Unfortunately, through some mistake, the pathologist neglected to take a specimen of the bone-marrow, but the spleen and lymph-glands showed practically a normal histologic picture. It seems quite evident, then, that these large dark blue staining leukocytes without evidence of granulation, nuclei rather indistinct and fusing into the protoplasm of the cell, are lymphoblasts or myeloblasts that have been called into the peripheral circulation as the result of the irritation produced by the pyogenic focus of infection. This brings up a very interesting discussion as to whether it is possible to have such a type of bone-marrow reaction, that it to say, is it possible to stimulate the bone-marrow by some peculiar toxin or poison so that unusual or abnormal cells are thrown into the peripheral circulation in large numbers? By analogy this is not impossible, while the contrary certainly is true, as Selling has shown that the leukocytes can be destroyed by specific leukotoxins. Occasional cases have been reported of this type such as I mention in which there is an abnormal myeloid reaction. The cases that I know about and those that have been reported have all been associated with prolonged and rather marked focal infection, such as this case. The gastric abscess had probably been present for a long time. When one sees cases such as this it calls to mind the fact that the whole subject of leukemia has not by any means been clarified, and that most certainly the etiology of the condition is not definite or finally completed. In connection with this case we have just

shown you I might say that Sternberg does not consider acute myeloid leukemia as an acute disease *sui generis*, but holds that the symptoms are due to systemic infection, especially caused by streptococci. Berblinger (Klinische Wochenschrift, July 15, 1922, p. 1449) recently reported 4 cases of acute myeloblastic leukemia, and he calls attention to the fact that in his cases the postmortem changes were in no way corresponding to those of sepsis. However, this finding does not negative Sternberg's contention, and in the present case would bear him out, as we had undoubted sepsis.

CASE II

The next case I wish to show you is a patient who died in the Presbyterian Hospital. The patient, B. S., aged thirty-three, was admitted to the Presbyterian Hospital November 12, 1921, and died January 30, 1922. She was admitted to the hospital complaining of pain in the back and back of legs. Her further history is as follows:

Present Illness.—Was operated on in the Presbyterian Hospital by Dr. Jopson last June for a growth in her jaw. The day before she left the hospital she first noticed this pain in her back and legs on going down the steps. Pain began low down in her back around the sacro-iliac joints, and in a week she was having pain over the whole of her back, but more severe on the right side. This pain became shooting in character and darting down her legs as far as the knees. About six weeks ago she began to have shooting pains from her back around her abdomen to the midline in front. Occasionally has slight shooting pains in both arms. This pain has not been constant until the past few days, since then it has been present continuously. She has no pains in the joints, and no swelling or redness, but occasionally knees get stiff, though she can bend them with some difficulty. This stiffness may last from one to two days to a week.

Since the onset of her trouble she has been very short of breath, especially on exertion. Has some slight swelling in ankles at night if she has been on her feet all day. Occasionally

has some palpitation. Has had no cough, until lately, when she "caught a cold," since which time she has had a slight cough, but no expectoration. No hemoptysis. Since her operation she has been having night-sweats, and for the past two weeks has had one every night.

Appetite good. Has no gastric symptoms since she had the operation for gall-stones three years ago. No nausea or vomiting. The bowels are constipated and she takes a saline every night.

The patient says she passes quite a large quantity of urine during the day, and has nocturia three to four times a night. No pain or burning on micturition.

Is rather nervous. Very easily excited. Some nights she sleeps well and others she does not. No headaches, except occasional "bilious headache." Since last June she has lost about 15 pounds in weight.

Has not menstruated for the past three years, following a pan-hysterectiomy for fibroids done at St. Joseph's Hospital.

Past Medical History.—Measles when a child. Operated on for "appendicitis" at fourteen years of age, and eight years later operated on for intestinal obstruction. Three years ago had a cholecystectomy and pan-hysterectomy. Last June had tumor removed from jaw.

Marital History.—Was married, but lived with husband only two years, and then obtained a divorce. Lives at a boarding house at present. Fair hygienic surroundings. Two cups of coffee or tea a day.

Family History.—Mother died from burns. Father died of pneumonia. No brothers or sisters.

Her physical examination I will not go into in detail. There was no gross adenopathy. Her lungs and heart were apparently normal. Her abdomen except for the old scar was practically normal. The liver and spleen were not palpable. The superficial reflexes were normal.

Clinical Summary.—This patient on admission to the hospital gave evidence of an osteo-arthritis of the spine, which was confirmed by Roentgen-ray, which showed marked absorption of the third lumbar vertebræ, absorption in second and fourth,

together with marked change and lipping along the edges of the body. When we went over the patient we also found that she had diseased tonsils and that there was one tooth diseased. Accordingly, two weeks after admission her tonsils were removed. These tonsils showed nothing bacteriologic, but streptococci. Shortly after this her arthritic condition seemed to improve considerably. We noted on admission that she had quite well-marked anemia and decided diminution in the number of polymorphonuclears. However, several blood-counts showed very little until the first one after tonsil operation, when hemoglobin had fallen markedly, while the leukocytes were much increased and the percentage of lymphocytes decidedly increased. From then on, as seen by the accompanying chart, a gradual increase in the percentage of lymphocytes took place as well as in the number of leukocytes. Shortly before death, about three months after admission, her leukocytes numbered 92,200, only 1 per cent. of which were polynuclears. The last few days of her life the hemoglobin was so low that it was impossible to estimate it. The type of cells that were seen under the microscope showed what were apparently small lymphocytes. The relatively small increase in percentage of large lymphocytes was indicative apparently of a chronic lymphatic leukemia rather than an acute type.

The type of cells, however, were, as in the first case, a type which did not appear to confirm the diagnosis of lymphatic leukemia positively, as they were not definitely lymphocytes, but rather they gave one the impression of being immature cells in which the several elements had not as yet had time to develop fully.

The physical examination of the patient also gave us no idea that leukemia was present. There was no enlargement of the superficial lymph-glands nor was the liver enlarged, while the spleen could not be palpated. The patient died finally as a result of the severe anemia from complete bone-marrow failure.

At autopsy, which will not be given *in toto*, there were seen a few superficial enlarged lymph-glands, but of the deeper glands

BLOOD EXAMINATIONS

Date.	Red cells	Leukocytes.	Hemoglobin.	Differential percentage. P.	L.L.	S.L	L.M.	T	E.	B.
11/ 2/21	3,660,000	9,400	60	34	24	22	19	1		
	Wassermann negative.									
	Blood urea N., 16.74 mgm. per 100 c.c.									
11/ 8/21	3,920,000	11,900	78							
11/10/21		8,950		40	25	22	8	1	1	3
12/ 4/21	3,340,000	14,500	46	15	66	9	7	1	1	
12/12/21	3,130,000	19,450	55	23	46	13	15	2		
				No myelocytes or megaloblasts.						
12/16/21	3,320,000	17,250	72	6	93				1	
12/21/21	3,100,000	14,500	49							
12/19/21	3,200,000	15,250	51	9	1	8			1	
12/24/21	2,630,000	16,350	52	10	16	79			1	
12/26/21	2,240,000	19,600	44							
12/28/21	2,010,000	18,600	35	7	48	41	2	1	1	
12/29/21	Platelets, 120,000; fragility; part. 45; comp. 375.									
1/ 1/22	1,920,000	22,950	41	4	3	91		1	1	
1/ 4/22	1,830,000	21,100	37	5	3	91			1	
1/ 9/22	1,690,000	22,050	20	11	2	87				
1/12/22	Platelets, 288,400; fragility; part. 45; comp. 35									
	B. U. N. 11.8 per 100 c.c.									
	B. uric acid 1.1 mgm. per 100 c.c.									
	Bleeding time, 4 mins., 20 sec.									
1/15/22	1,350,000	25,100	21	4	3	91		1	1	
1/23/22	1,120,000	42,200		2	5	93				
1/27/22	1,100,000	92,200		1	2	97				
	Blood-platelets, 200,400.									

only the retroperitoneal lymph-glands were much enlarged. The liver weighed 1600 grams, the capsule smooth, not thickened, the edges sharp, consistency decreased, color yellowish. On cut section the organ was apparently bloodless. The liver lobules could be plainly made out and were brownish-yellow in color.

The spleen weighed 480 grams, capsule smooth, not thickened, and the whole organ was a mottled pale grayish-red with irregular purplish patches. The follicles could be made out easily, were apparently increased numerically, but did not exceed the size of a pinhead. Pulp itself was soft.

In this case we have the development of leukemia in a patient who came into the hospital apparently free from the condition. Associated with this leukemia was a marked aplasia of the bone-marrow, which apparently was the cause of the

patient's death rather than the leukemia. Her hemoglobin and red cells fell steadily from the time she was admitted. In view of the fact that she had an arthritis and the possibility of focal infection, the teeth, tonsils, and sinuses were carefully examined. Tonsils showed the only evidences of infection that could be found. They were distinctly diseased and on culture showed Streptococcus viridans, non-hemolytic streptococcus, and Streptococcus albus and aureus.

In this patient, then, we have a secondary infection severe enough to produce a severe arthritis (the arthritic symptoms improved after the removal of the tonsils). Whether this secondary infection bore any relation to the acute leukemia is a question difficult to answer, as our knowledge of the pathogenesis of leukemia is decidedly hazy. There are several theories to explain the causation of the disease. It would be necessary were we to incriminate the infection to accept the idea that leukemia is a result of infection rather than, for example, the manifestation of a circulating neoplasm. However, it does not seem unlikely in this case that the infection bore some relation to the disease, and, furthermore, the infection seemed to show a quite marked tendency to cause degenerative changes in the erythrogenic elements of the hemopoietic system. There was apparently complete inability of the bone-marrow to respond by the production of red cells. On the other hand, we have the anomalous condition of failure of the bone-marrow to produce red cells through exhaustion, though able to throw out a large number of young leukocytes into the peripheral circulation.

SUMMARY

These 2 cases are shown you with the idea of demonstrating that in no sense is leukemia a clear-cut disease entity which always runs the same course, as is the usually accepted conception of the disease. Bizarre and abnormal manifestations of the disease take place, and these deviations from the normal tend to confuse the etiology of the disorder. There is no definitely proved cause of leukemia. Leukemic-like reactions occur in a certain number of cases with, or in association with, septic processes within the body.

CLINIC OF DR. HENRY K. MOHLER

JEFFERSON MEDICAL COLLEGE

THE VALUE OF BASAL METABOLIC STUDIES IN THE DIFFERENTIAL DIAGNOSIS OF CONDITIONS RESEMBLING HYPERTHYROIDISM. PRESENTATION OF FOUR CASES ILLUSTRATING ITS VALUE

IN considering the aid which the knowledge of the basal metabolic rate can be in the differential diagnosis of mild or moderately severe cases of hyperthyroidism, and other conditions which resemble it, I will refer only to one of the several of its uses in the field of medicine and surgery.

The estimation of the metabolic rate and its consideration in connection with the diagnosis and the treatment of disease processes is of value in the light of our present knowledge of the subject, as follows:

1. As an aid in the recognition of diseases which have as a cardinal feature an increased or a decreased basal metabolic rate. To aid in the differential diagnosis of conditions which resemble each other in symptomatology and physical findings except in the basal metabolic rate.

2. As a guide to the proper kind of treatment, medical, surgical, *x*-ray, or radium, and to measure their effectiveness.

3. The basal metabolic rate in disturbances of the thyroid gland, all other things being equal, is of value in determining the degree of the disorder of function of the thyroid gland. It will not determine the degree of any associated circulatory disorder.

It is incumbent upon every practitioner of medicine to early recognize diseased conditions, and, if possible, in the very incipiency of the process. The efforts of the medical profession

are directed toward discovering practical means to assist in making the early diagnosis possible. The development of apparatus for the practical determination of the basal metabolic rate is an advance in the proper direction.

Three diseases commonly confused and ofttimes most difficult to differentiate until they are beyond the early stage are mild or moderately severe hyperthyroidism, early pulmonary tuberculosis, and the condition known as "effort syndrome," or, as it is called, neurocirculatory asthenia, and also sometimes referred to as "disordered or nervous action of the heart."

These patients are presented to illustrate various conditions whose identity was established even as to degree by means of basal metabolism studies. It is not to be inferred that every case which one is called upon to study will be solved as readily by the basal metabolic rate determination as in the cases to be cited.

CASE I

The patient, M. S., is twenty-two years of age, married, and the blond type. She was born and had always lived a very active life in Philadelphia, Pa. Shortly after she was married, about two years ago, her husband was transferred by his employers to a small town 40 miles from Philadelphia. Here, because of the different surroundings to which the patient had been accustomed, she became lonely and discontented. From a healthy and robust young woman, she became nervous, lost weight, developed frequency of urination, suffered attacks of diarrhea, manifested tremor of the hands, and tachycardia. Her appetite was excellent and she slept fairly well, but had difficulty in falling asleep. After consulting several physicians and undergoing their medical treatment, with no results, she consulted a physician in a nearby city, who, during the course of a complete physical examination, noticed a symmetric enlargement of her thyroid gland. He diagnosed her symptoms as being due to hyperthyroidism. The mother of the patient stated that the thyroid gland had been enlarged since the onset of puberty, but that recently she believed it had increased in size. The physician advised *x*-ray treatment for the enlarged

thyroid gland. After receiving one treatment the patient's "nervousness" seemed to have been aggravated. The patient, following the first *x*-ray treatment, came under observation at the hospital, where the foregoing information was obtained and the following notes were made:

The patient is very nervous and apprehensive. The pupils of the eyes react normally to light and accommodation and are widely dilated. The teeth and tonsils showed nothing worthy of note. The thyroid gland is uniformly enlarged. No bruit or thrill or enlarged veins are noted in connection with the gland. The heart and lungs are negative except for the heart-rate, which is 130 per minute. The abdomen is negative. The knee-jerks are plus and a tremor is present in the extended arm and spread hand. The examination of the urine is negative except for a low specific gravity—1.008. The blood count is normal. The temperature is 98.2° F. and the pulse-rate is 130 per minute. The blood-pressure is 120/80. The blood Wassermann is negative. Her weight is 118 pounds, which is 12 pounds less than one year previously.

Discussion.—The problem that confronts us is, are we dealing with a nervous high-strung patient in the usual accepted sense of the word—or is the patient an early diabetic, as her condition had been diagnosed, or are her symptoms due to increased or abnormal activity of the thyroid gland? The treatment of hyperthyroidism, surgically, with radium or with the *x*-ray is not free from danger if the condition has been incorrectly diagnosed. Additional light on the patient's condition was sought and the determination of the basal metabolic rate was ordered. The patient was so nervous that the first two tests were a failure due to her inability to co-operate. The third, fourth, and fifth tests were very satisfactory, in that the patient co-operated splendidly and the results were uniform and all within the range of normal. A nervous, high-strung patient, with a course tremor, a tachycardia, with a normal basal metabolic rate carefully determined on three different occasions, and other findings negative except for goiter, warranted a diagnosis of a functional nervous disorder and not a

thyroid gland disturbance. We so advised the patient. A change of scene and bromid of soda, 10 grains three times daily, were ordered. After two weeks' treatment, under the care of her physician, at the home of her mother in Philadelphia, which consisted of rest in bed, concentrated nourishing food, with bromid of soda as directed, the patient improved in every way. Her weight increased, the heart-rate became less rapid, so that the pulse-rate was seldom more than 90 per minute. The frequency of urination had almost disappeared, as well as the tremor. Six weeks later the patient had entirely regained her previous normal health.

The thyroid gland did not increase or decrease in size and was not etiologically related to her symptoms.

If the patient had had hyperthyroidism, as the condition was diagnosed, the *x*-ray treatment should have been of benefit to her. On the other hand, *x*-ray treatments were contraindicated, and if continued would have caused much harm.

The knowledge of the basal metabolic rate was the deciding factor in changing the previously made diagnosis and the treatment.

CASE II

B. L. is the sixteen-year-old daughter of a physician, the only child living out of a family of 4. The father became greatly concerned because of the symptoms which appeared rather suddenly. The case is most interesting and the history is as follows:

The **family history** is negative.

Personal History.—During childhood the patient had measles, chickenpox, and scarlet fever. The child was normal and healthy until the age of twelve years, when she began suddenly to take on weight, becoming, as her father stated, obese. Her face, neck, and arms became very stout and pads of fat were present. The patient did not suffer any pain. The child became somewhat less active both mentally and physically. After consulting several physicians the father was told that the child did not require any treatment, and that she would improve with the onset of puberty. Shortly before

the patient's sixteenth birthday she began to menstruate. Within a period of three months following the onset of the first menstruation the following changes took place: the child lost 15 pounds in weight, the thyroid gland increased very noticeably in size, and the mental condition improved. The patient became very nervous, irritable, slept poorly, ate ravenously, became almost uncontrollable at times, so far as her restlessness and talk were concerned. Occasionally she seemed to be mentally confused and frequently complained of "rapid heart action," Her eyes became prominent, and her pulse, which before the onset of puberty was 75 to 80 per minute, now ranged from 100 to 130 per minute. The patient at this time came under observation, the previous history was obtained, and the following notes were made of the physical findings:

It is evident that the patient has lost weight, but continues to have superfluous fat. She is very nervous during the examination and perspires freely. The patient's eyes are prominent and have a "frightened" appearance, otherwise they are negative. The thyroid gland is uniformly enlarged and pulsates to a small degree. The lungs are negative, as is the heart, except for its rapid rate.

The abdomen is negative. Extremities: It is difficult for the patient to keep her hands quiet, but no tremor is present. The temperature was 97.6° F. The pulse-rate was 120 per minute. The blood-pressure was 105/85. After a preliminary test to acquaint the patient with the procedure for the determination of the basal metabolic rate, three tests were performed on each of alternate days, with the following results, −12, −15, −15. Subsequent blood-counts and urinary examinations were normal.

Discussion.—It is needless to say that we were surprised to obtain minus basal metabolic rates. Any rate which is within the range between −1 and −15 is considered normal. The father feared that with the advent of puberty the child had suddenly developed acute hyperthyroidism (which, of course, in a sense was true), and that the condition would continue and, unless checked, result fatally. He was very anxious to have the child

receive promptly either surgical or *x*-ray treatment. It was only after considerable persuasion that he consented to have the child put to rest in bed with an ice collar to her neck, and the administration of sedatives, codein sulphate, and bromid of soda. This treatment was continued for six weeks, with a determination of the basal metabolic rate weekly. The patient's condition improved in every way except for her metabolic rate. Nearly six months have now elapsed and the basal metabolic rate continues to range from −5 to −10. The patient continues to be somewhat overweight, the pulse-rate normal, 72 to 76 per minute, the mental condition is good, and the extreme nervous tension has disappeared. The thyroid gland is somewhat smaller, but is still larger than normal. If the basal metabolic rate continues to be low, and the patient's symptoms do not continue to improve, we will suggest the patient be given thyroid extract, beginning with ½ grain three times daily.

Our conclusions were that this patient was suffering from insufficiency of the thyroid gland secretion, and possibly from disturbance also of other glands of internal secretion which would account for the delay in the onset of puberty, the obesity, and disturbed mental state. Suddenly the thyroid became very active to meet the body demand. The suddenness, while it had a beneficial effect, caused symptoms of thyroid intoxication to develop. These symptoms became alarming, because, although the body needed additional thyroid secretion, it was thrown into the circulation in quantities greater than the body could readily utilize. To have interfered with the thyroid gland by the treatment desired by the patient's father would have been to permanently lessen the activity of the thyroid gland and would have defeated nature's purpose. That no harm was done by not interfering surgically or by *x*-ray treatment is evident. The evidence was made more convincing in view of the repeated minus basal metabolic rates which were obtained.

CASE III

The patient, F. E., is thirty-two years of age, married, and by occupation a mail carrier. The chief complaint is shortness

of breath and the "heart beats too rapidly." The family history is negative.

Present History.—The patient had measles, mumps, chickenpox, and whooping-cough during childhood. His general health always was good and he was accustomed to considerable exercise. He gives no history of any venereal disease. He never used alcohol; uses tea, coffee, and tobacco in moderation. His appetite is good and his bowels are regular. In 1918 he had an attack of influenza which kept him from his duties for nearly two months on account of subsequent weakness.

Present Trouble.—Nine months ago the patient noticed that his neck was increasing in size so that he had to wear a collar one-half size larger. His wife also noticed that his eyes seemed more prominent than before and that he stared frequently, which he had not done previously. He complained of shortness of breath while about his duties, even when walking slowly on the level, and of a throbbing in the neck. He then consulted "an adjuster of the spinal column" and took a number of treatments. He became worse, especially did the "throbbing" in his neck and the shortness of breath increase. He was then advised to give up his work and rest for three months, which he did, with benefit. On returning to work the throbbing in his neck and other symptoms complained of became worse, and he consulted a physician, who advised him to apply for admission to the hospital ward, which was done. The following notes were made:

The patient has to be propped up in bed in order to breathe comfortably. There is no evidence of cyanosis or edema. Head: The eyes are prominent, palpebral fissure not widened, and no other evidence of exophthalmic goiter, so far as the eyes are concerned, is present. His teeth are in good condition. The tonsils are small and embedded. Neck: There is a uniform enlargement of the neck and the thyroid gland. The vessels in the lateral aspect of the neck and over the suprasternal notch pulsate markedly, and thrills are palpable over these areas. The fulness of the neck is accentuated by the vascular engorgement.

Chest: The chest is well developed and his expansion is equal. The lungs are clear and resonant throughout and no râles are heard. Heart: The apex-beat is visible in the fifth and sixth interspaces in the anterior axillary line. No thrill is palpable over the precordium. The left border of cardiac dulness extends to the left anterior axillary line in the sixth interspace and the right border is at the right sternal border. The dulness over the base of the heart is increased on either side of the manubrium sterni. The fluoroscopic examination made later showed this to be due entirely to the aorta, which is dilated. A systolic murmur and a diastolic murmur are heard in the aortic area, the latter well transmitted over the entire anterior wall of the left chest. A systolic murmur is heard at the apex, which is transmitted to the axilla. The pulse is collapsing. The abdomen is negative. The extremities are negative. No recognizable tremor is present. The urine is negative and the blood-picture shows a slight secondary anemia. The blood Wassermann is negative. The temperature is normal and the pulse ranges from 100 to 130 per minute. The blood-pressure is 160/20.

Discussion.—The problem was, how many of the symptoms presented, if any, were due to hyperthyroidism, or were all of his symptoms due to his aortic disease, or are both conditions present and, if so, to what degree? The patient was kept at absolute rest in bed and given tincture of digitalis in doses of 15 to 20 drops three times a day for a period of twenty-five days. At the end of this period the patient seemed slightly better, but he did not improve to the degree one would expect. There was no question that the patient had impairment of his cardiac function, but did his thyroid gland, which gave some evidence of hyperactivity, aggravate the cardiac condition?

In view of the somewhat weak evidence—viz., the enlarged thyroid gland and the rather prominent eyes—it was thought that the patient might be also suffering from hyperthyroidism. While the gland was enlarged it must be remembered that in aortic regurgitation the neck becomes enlarged, due to increased engorgement of the vessels. The eyes also appear prominent

at times in aortic regurgitation in the absence of hyperthyroidism.

As an aid to help to decide these questions the determination of the basal metabolic rate was ordered. On three occasions a rate between +40 and +45 was obtained. With these findings and the other symptoms and the failure to improve sufficiently with treatment for the cardiac condition, the patient was advised to have ligation of the superior thyroid artery on one side of the neck only. Almost immediately after the operation he seemed to improve and his metabolic rate dropped to +25 at the end of a month. Then the other side was ligated, and three weeks later the basal metabolic rate was reduced to +15. The patient, seven weeks after the preliminary ligation, states that he is more comfortable than he had been for nine months, or since the onset of the present trouble. He does not appear to be nervous, his pulse ranges from 90 to 95 per minute. His eyes and the thyroid gland have changed but little. He can sleep with comfort on three pillows. Additional surgery may be indicated if the patient does not continue to improve, but the lesson to be learned is that once sure that the thyroid gland is overactive, surgery, with its risk, was indicated. The basal metabolic rate was the deciding factor. In doubtful cases valuable information can be obtained by a study of the basal metabolic rate.

The findings in the case raise the question as to whether or not the increased turgescence, which apparently is present in the neck in aortic regurgitation, can excite the thyroid gland to increased activity.

There is a resemblance at times between the symptomatology and physical signs, especially in so far as the circulation is concerned, between aortic regurgitation and thyroid hyperactivity.

CASE IV

The patient, F. R., is a Hebrew, twenty-nine years of age, married, and the mother of 2 healthy children. She came to the out-patient department of the hospital complaining of a loss of weight of 14 pounds during the past year, a slightly

productive cough, which has been present since an attack of pleurisy ten years ago. The patient also complains of being nervous.

The **family history** is negative except that her mother and one brother have died of heart disease.

Personal History.—The patient does not recall having had any of the diseases common to childhood, and until her attack of left-sided dry pleurisy was in good health except for frequent attacks of tonsillitis. The tonsils were removed about two years ago.

Present Trouble.—The patient states that the operation for the removal of her tonsils (which was performed under local anesthesia because of her history of pleurisy) was quite a shock, and that her health has been impaired since. Almost immediately following the tonsillectomy she complained of a cough, which is slightly productive; she feels feverish at times, has a poor appetite, has lost in weight and strength, and is annoyed by nervousness and excessive perspiration.

Physical Examination.—The eyes and mouth are negative. The neck shows visible pulsation in the lateral aspects and the thyroid is palpably enlarged. The patient states this enlargement has been present since the menstrual periods have been established. The chest is of the phthisical type, expansion is shallow, but equal. There is no impairment of the percussion note; the breath sounds are poorly heard at the left base posteriorly. In the upper left chest posteriorly the breath sounds are harsh and a few crackles are heard. Nothing abnormal is heard on the right side. On examination, the abdomen and extremities are negative. The temperature at 3 P. M. is 99.1° F., the pulse-rate is 120 per minute, and the respirations are 20 per minute. Her weight is 108 pounds, which is 14 pounds less than one year ago. The sputum examination was negative for tubercle bacilli on five different occasions. The *x*-ray examination of the chest shows evidence of an old tuberculous lesion at the left apex. The urine is negative and the blood-count normal. The blood Wassermann is negative.

Discussion.—The patient is very much worried and fears

she has tuberculosis; in fact, she has a phobia on this subject. She has consulted a number of physicians and medical out-patient departments, and she states the diagnosis that was given her was slight tuberculous activity of the left lung. The out-patient department of the hospital sent the patient to the ward for further study, and her record showed that her maximum daily temperature during rest in bed varied from 99° to 99.8° F., with a pulse-rate ranging from 100 to 129 per minute. Her basal metabolic rate was determined on three different occasions during the second week of her hospital stay and the basal metabolic rate was +45, +38, and +39. She was discharged from the hospital reassured that her lung lesion was not responsible for her symptoms, that she had some slight trouble with her thyroid gland. A high caloric diet was ordered, with *x*-ray treatment of the thyroid gland. Three months later the patient's temperature was normal on three successive days. She had gained 10 pounds in weight and was feeling very much better in general. She was not nearly so nervous and her cough had become much less. Unfortunately, we have not had the opportunity to make further basal metabolic studies. The patient undoubtedly has an old tuberculous lesion at the apex, but the deciding factor in making our diagnosis was the result of the basal metabolic studies.

We are convinced of the value of the basal metabolic determinations in arriving at a diagnosis in these borderline cases, the symptomatology of which is very similar in many respects.

Frequent determinations of the basal metabolic rate in young women who have enlarged thyroid glands and who complain of being nervous will usually furnish evidence for or against the necessity of instituting treatment for the enlarged thyroid gland, a condition which often causes unnecessary anxiety.

CLINIC OF DR. ROBERT G. TORREY

PHILADELPHIA GENERAL HOSPITAL

ANEURYSM OF THE AORTA, WITH REMARKS CONCERNING THE EFFECTS OF ANEURYSM ON THE CORONARY CIRCULATION

IN general, the cardiac cases which have been shown here are about equally divided between inflammatory conditions, of which rheumatic fever is the typical and chief infection concerned, and degenerative conditions due to syphilis, arteriosclerosis, and the hypertrophy of chronic renal disease. There have been shown this season 3 cases of aneurysm which have previously been wired, and a number of aneurysms not thus treated.

In considering the question of aneurysm, we too often consider the aneurysm as the only important factor in the case, forgetting that the aortic dilatation may be simply an incident in the course of generalized cardiovascular syphilis. The aneurysm may be the most important factor and the one which threatens the life of the patient, and it is true that many cases terminate by rupture of the sac or through exhaustion incident to tracheal pressure or irritation of the recurrent laryngeal nerve, but observation of the many cases of aneurysm in the wards forces us to the belief that the termination in the majority of these cases is similar to that observed in other types of luetic cardiac disease and is the result of myocardial failure.

Many aneurysms threaten external rupture, but few accomplish it. Often we see a huge pulsating bulging of the chest, the skin thinned and discolored, and it seems as though each beat of the heart would force the blood through the frail wall. Many of these cases, of course, rupture internally, but arrest of the heart in an attack of angina or gradual cardiac decompensation are probably more common endings. I have questioned

nurses in charge of the Men's Medical Wards who must have had charge in the aggregate of scores of aneurysm cases, and none of them had seen an external rupture.

It has not been clearly demonstrated that aneurysm in itself causes any great increase in the work of the heart or causes hypertrophy. Most cases of aneurysm are preceded or accompanied by a generalized arteriosclerosis and cardiac hypertrophy, but it is my belief that aortic aneurysm in itself interferes with the proper delivery of blood by the coronary system, thus hastening the process of myocardial degeneration and cardiac breakdown. Angina is so usual in these cases and myocardial degeneration so rapid that this view seems reasonable. This view of the matter throws further light on the puzzling question as to why all large aneurysms do not rupture. As the sac becomes larger and more distensible the coronary circulation becomes rapidly less efficient and myocardial failure more and more imminent.

Pain is a prominent and perhaps the most constant symptom in aneurysm. Pain is apt to occur in aortitis before dilatation is marked. This type of pain is usually not severe, is aggravated by exercise, and is referred to the region of the clavicle and base of the neck on one side or the other. The late Dr. Frederick Klaer made a very complete study with *x*-ray control, of a series of patients at the Medical Dispensary, exhibiting aortitis with characteristic pain and with beginning or suspicion of beginning enlargement of the arch.

Severe pain may be caused by pressure and erosion, but even enormously destructive aneurysms may cause comparatively little pain of this type.

The most constant and typical pain in aneurysm is angina pectoris. It is easy to overlook this point and to consider the pain as due to pressure, but you will find that the pain in aneurysms of the ascending arch which point to the right is commonly referred to the left shoulder or precordium, and frequently down the left arm, and paroxysms of agonizing pain which are perfectly typical of severe angina are frequent. Does angina indicate an insufficient blood-supply to the myocardium?

Probably that is its usual significance. Does an aneurysm of the arch interfere with the proper or favorable delivery of blood to the coronary system? It is not only conceivable but seems probable that a profound change in conditions relative to the coronary supply takes place as a result of the relatively rigid aorta of limited capacity being replaced by a comparatively voluminous and easily distensible sac whose walls yield to each thrust of the ventricle. The effects of changes in the character of the vessel walls, in the capacity of the aorta, in the content of the capillary field, are complex, but cause striking changes in peripheral blood-pressure and in the form of the pulse tracing. The effect on the coronary blood-pressure resulting from the replacement of the aortic tube by an aneurysmal sac should be easily demonstrable. Apart from the simple question of blood-pressure, changes in the form of the pulse wave are to be looked for which may indicate an alteration in efficiency of the coronary circulation.

The prompt relief of pain which takes place when an aneurysm is wired and a suitable current passed through the wire coils in the sac can best be explained on this same basis. The introduction of a large clot into the sac reduces the fluid content of the aneurysm and alters conditions of coronary circulation. The improvement in cardiac condition and disappearance of angina following this operation as noted by Dr. Hobart Hare in his large series of cases, and as observed in the cases of Dr. Sailer and others in this hospital, would seem to be best explained on this basis.

You have seen the operation of wiring in Dr. Sailer's clinic and are familiar with the details of the operation. These patients have had wiring done by Dr. Sailer, Dr. Musser, and myself. The result may be said to have been unqualifiedly good in one case and to have afforded temporary relief from pain and discomfort for several months in the other cases.

One of these patients was admitted to Dr. Sailer's service several years ago, and an aneurysm of the left subclavian artery and arch of the aorta was wired at that time by Dr. Sailer. The aneurysm had previously been exposed by a surgeon who

proposed to do a Matas operation on the subclavian, but finding the wall of the arch involved in the sac, this plan was abandoned. An interesting feature in this case was the development of clubbing of the nails on the left hand. Prior to the first wiring the left arm was cyanotic and puffed, and clubbing of the fingertips progressed rapidly while the patient was under observation in the course of a few weeks. The swelling and cyanosis of the arm cleared up at once after wiring. It was evidently due to pressure on the subclavian vein. The immediate effect of wiring was a relief from severe pain which occurred when the current was turned through the wire, and within a day or two the bulging was greatly diminished. Two subsequent wirings were done for extension of the aneurysm toward the axilla, with relief on each occasion. The last time the patient was seen he came to the hospital on account of pain in the left side, but reported that he had been working as a farm hand all summer doing a full day's work comfortably, this being about six years after the first operation.

The other two wired aneurysms were diffuse swellings involving particularly the ascending arch, and were entered from the right side. Relief of pain was satisfactory in both cases, but there has since been a return of symptoms in each case.

The results in wiring these aneurysms may be said to have been good in that there was reduction in the size of the swelling in each case, reduction of pulsation, and, most important, an immediate relief of pain. Two of these patients were wired once, one of them three times during about three years. Wiring of the sac is a comparatively simple procedure in suitable cases and the immediate subjective relief is usually very striking.

Dr. Hare states that only saccular aneurysms are suitable for this treatment. As Dr. Stengel has pointed out, in many cases of aneurysm bulging anteriorly the tumor is a false aneurysm lying anterior to the ribs and not the main sac emerging through erosion, and these cases which look so desperate should be particularly favorable for this method of treatment.

I have seen 3 cases come to autopsy. In none of them was the clot organized or firm or adherent enough to afford any

support to the aortic wall, but all of them had shown improvement in condition which was surprising, one patient wired by Dr. Sailer doing the most strenuous kind of work for a number of months before his death, though death from exhaustion and cardiac failure seemed imminent at the time of operation.

I do not wish to advocate the general use of this operation. We do not understand indications for its application. It has been employed thus far for relief of intolerable pain, and in many cases the results have been much better than was expected. It is a radical procedure, but bad results have been unusual. One might expect a prompt development of embolism, but such cases have not been reported. It may be that some such method of treatment is capable of wider application than we now realize, but I believe that it should be studied in the physiologic laboratory from the point of view of the effect on the coronary circulation. It has, of course, no tendency to cure the aneurysm. Needling the sac, as advocated by MacEwen, theoretically tends to obliterate the sac by forming white clot, which organizes, while wiring causes the formation of red clot only.

There is, of course, no satisfactory treatment for aneurysm except in rare instances, and rarely aneurysm may do well untreated for many years. Saccular aneurysms may occur which are traumatic or the result of purely local weakening of the aorta and be coexistent with a relatively healthy heart and vascular system. This condition is unusual. If such an aneurysm is relatively small, it may exist for a long time without symptoms or signs. These aneurysms are usually discovered by the *x*-ray or at autopsy.

Aneurysms of the descending aorta may attain considerable size and cause marked pressure symptoms before the heart is seriously affected. They are often difficult to demonstrate by physical signs. Aneurysms involving the first part of the aorta may show serious cardiac involvement before the sac attains any great size. They can usually be easily demonstrated by physical signs and probably affect the coronary circulation more than do the others.

Another phase of luetic disease of the heart and aorta which I wish to discuss is the bad result often seen after the administration of arsenical preparations. The danger of salvarsan treatment in these cases, though frequently mentioned, is not sufficiently emphasized. Dr. Udo J. Wile recently published a paper on this subject in the American Journal of the Medical Sciences (September, 1922) which can be read with profit by all of you. A few years ago there was much more careless use of salvarsan in these cases than is seen today, but we still see patients with aortitis and cardiac disease due to syphilis, who were in good condition prior to salvarsan administration, showing rapid dilatation of the heart and cardiac breakdown after such treatment. It may be that rapid obliteration of redundant tissue as a result of treatment suddenly removes some support from the muscle-fibers of the myocardium, or there may be a toxic effect on the cardiac structures analogous to the nervous tissue reaction observed in cerebrospinal syphilis so treated. We do not understand the processes involved, but experience shows the need of extreme caution in the use of salvarsan and the need of restricting the dose to the minimum limit if it is to be used at all. Small doses of iodid seem useful in many cases and mercury in moderate dosage safe.

CLINIC OF DR. C. C. WOLFERTH

UNIVERSITY HOSPITAL

ARTERIAL BLOOD-PRESSURE IN HEART DISEASE

TODAY I wish to discuss with you effects of various forms of heart disease on arterial blood-pressure. We all recognize the fact that the pumping action of the heart supplies nearly if not quite all the force of the pressure the blood exerts against the arterial walls. But the mechanism that governs the heart's action is delicate and complicated, and although the work of experimental physiologists in this field has revealed much, there is a great deal still to be explained. Blood-pressure in every part of the circulatory path is constantly changing every moment and, moreover, is subject to a great variety of influences which modify the effect of the pumping action of the heart. If the extracardiac mechanisms fail to do their work properly, there is evidence that the heart attempts to take on the extra burden of carrying on the circulation. If the heart is not capable of doing its part, its work may be made easier by compensatory action on the part of the other agencies concerned in maintaining the circulation. In these adjustments the tendency may be to keep the blood-pressure near normal, or it may be greatly altered, as in such well-known instances as arteriosclerosis and aortic regurgitation.

It is extraordinary to what an extent the clinical literature abounds with simple, plausible, but, unfortunately, unverified explanations of various alterations in blood-pressure from the normal. We must not accept these attractive speculations at their face value. Our real knowledge of this subject has gone forward step by step by the correlation of the results of clinical observation with the data acquired by experiment.

It may be instructive to recall a few of the older studies of the circulation and note how reasoning based on speculation rather than fact has led to grotesque error. Borelli, an eminent mathematician, calculated the force of the heart at 135,000 pounds (De Motu Animalium, 1680), while Keill, a mathematician equally eminent, calculated it at 16 ounces (Animal Secretion, etc., 1708). Flint, in commenting on these discordant results, raises the question as to why they went so far wrong, and concludes that it was because they paid so much attention to mathematics that they overlooked the necessity for practical experiment and careful observation.

The Rev. Stephen Hales, who has been called the founder of experimental physiology, began his work on the basis of no more knowledge regarding the circulation than Borelli or Keill, but as a result of experiments in which blood-pressure was measured for the first time (Statical Essays, 1733) he arrived at conclusions regarding the force of the heart action not so very different from those held today.

Hales' notable experiment in measuring blood-pressure was performed on a mare. The method consisted of the insertion of a brass pipe with a long glass tube connected to it into the femoral artery of the mare and then the measurement of the height to which the column of blood ascended within the tube. The first improvement in this method came nearly a century later when Poiseuille introduced a U-shaped mercury manometer for measuring pressure (Rech. sur la force du cœur aortique, 1828). Ludwig invented graphic methods of recording pressures, and to him we owe not only his own notable contributions, but the interest he aroused in the subject. Vierordt in 1855 was the first to introduce a method for the estimation of pressure without opening an artery, and to him, therefore, belongs the honor of paving the way for clinical study of the subject.

Vierordt's method consisted of applying pressure to an artery and noting the amount of pressure necessary to obliterate the pulse below. This method was improved by von Basch (1876) and Potain (1889), both of whom aroused clinical interest in the subject. The principle of the present-day method of meas-

uring arterial pressure we owe to the genius of Riva-Rocci, who introduced the pneumatic cuff and used a mercury manometer to measure the pressure exerted in it. Riva-Rocci's method quickly became popular. Systolic pressure was recognized satisfactorily by noting the return of pulsation in the artery below. Oscillation methods were devised to measure diastolic pressure, and these are still widely used, particularly in Europe. The auscultatory method of measuring pressure, which you all use, was suggested by Korotkow in 1905. Thus far it has not been improved.

I have here mentioned only some of the most notable advances in the technic of measuring arterial pressure. You should, however, recognize the fact that the simple procedure you use is based on an enormous amount of research in which every detail of the method has been subject to searching examination. It is recognized by the workers in this field that there are obvious sources of error in the determinations, and possibly others not yet recognized. Therefore, in view of the clinical importance we have come to attach to blood-pressure findings, it is of importance that we use the best apparatus available and care in our technic.

Careful experiments have shown that the proper width of cuff for measuring brachial pressure in adults is 12 cm. In children a narrower cuff is permissible. A mercury manometer should be employed rather than one constructed on the aneroid principle. With the former, if unexpected readings are obtained, one does not need to wonder whether or not the apparatus is out of order. They are now made to fold up in small compact boxes easily carried, so that the excuse that the aneroid gages are more convenient is of little importance.

The cuff should be applied snugly, but not too firmly, about the arm. If it is too tight the readings will tend to be too low, and if it is too loose, they will tend to be too high. Before pumping air into the cuff the scale by which the height of the column of mercury is read should be inspected to see that the zero point corresponds to the top of the column of mercury. Failure

to do this is a frequent omission, and inaccurate readings to the extent of 5 to 10 mm. result not uncommonly.

The auscultatory method of reading pressure is generally accepted as the most accurate, but should be checked against invariably by palpation of the radial pulse. The systolic pressure determined by the latter method is usually a few millimeters lower than that found by auscultation. If this is not the case, you should look for some error in technic. It is usually due to faulty position of the stethoscope in relation to the brachial artery. Occasionally, however, there may be a phase between systolic and diastolic pressures during which no sound is heard over the artery. In such cases there is a possibility of reading the systolic pressure far too low if one does not check the reading by the palpation method.

You are all familiar with the fact that as one listens over the artery the character of the sound changes as the pressure is released. An effort has been made to subdivide, according to the character of these sounds, the pressure between systolic and diastolic into a number of phases. Some have attempted to attach clinical significance to these phases and their variations. Thus far such claims have not been established, and we need discuss them no further here.

The point at which diastolic pressure should be read is important. The work of MacWilliam and others appears to show conclusively that it should be read at the instant of abrupt change in character of the sound over the artery from loud, sharp, or murmurish to faint. There are some who believe that complete disappearance of sound corresponds to true diastolic pressure, but MacWilliam's experiments show that the faint sound persists after beginning flattening of the lumen of an artery by pressure.

One should always make several readings of both systolic and diastolic pressures not only as a check on accuracy but also to discount, as far as possible, the effect of excitement on the part of the patient. Moreover, in the case of rigid arteries, repeated compression and decompression tends in some instances to lessen the resistance of the vessel wall.

Even after we have made our determinations with the greatest care there are sources of error we are unable to control. Outstanding factors are variations in thickness and resistance of the soft parts of the arm and in the arterial wall. A German writer has recently proposed that we stop calling the maximum reading we obtain systolic pressure, and substitute therefore "Pulssperrdruck" or pulse-obliterating pressure, for the latter is what we measure and may be quite different from true systolic pressure.

Sahli, whose name has long been identified with blood-pressure research, has severely criticized cuff methods of determining blood-pressure, particularly diastolic pressure. He states that diastolic pressure in the vessel being tested is greatly elevated by obstruction of venous return by the cuff. He advocates that blood-pressure be determined by direct pressure of a pelotte over the radial. The pelotte is connected with an ingenious device which is, in effect, a very delicate oscillometer.

While Sahli's contentions thus far have not been established, we should bear in mind the imperfections of the standard method used today, and the possibility that the errors by this method are even greater than we suspect. Nevertheless, it has been so widely employed by clinical workers and so much valuable clinical data has been accumulated, that the wisest course would appear to be continuance of its use until some other method has been clearly shown to be better. In the meantime we should be cautious in our interpretation of results and maintain an open mind in respect of further research on the subject. It must be remembered that, at best, we obtain only approximations of maximum and minimum pressures, which do not tell the whole story even of arterial pressure. One does not need to be very conversant with sphygmograms to realize to what an extent average or mean pressure, which is regarded by physiologists as the most significant measure of the force with which the blood is driven through the arteries, may vary with identical systolic and diastolic readings.

If we bear in mind the manifest and potential sources of error in our determinations of maximum and minimum pressures in

the brachial artery, some of which have just been indicated, and the fact that these figures do not indicate accurately the mean arterial pressure; if we remember that various extracardiac mechanisms modify pressure profoundly and may exert action in such a way as to ease the burden on the heart, or, indeed, in the opposite direction, it becomes apparent on what an insecure foundation attempts to estimate cardiac function from arterial blood-pressure figures rest. At any rate, it seems clear that we have not yet advanced far enough in our knowledge of blood-pressure and its relation to the circulatory mechanism to use such figures as we are able to obtain clinically to calculate the cardiac function in abnormal states.

Apparently the very obvious fact that arterial blood-pressure owes its origin to the heart pumping blood into the arteries has led to a number of assumptions as to how this may be altered in disease. Many of our writers on this subject have tried to make it appear too simple. I wish to emphasize to you that one cannot even make a start in the study of arterial pressure in heart disease without evaluating such factors as may modify it in any individual case, such as disturbances in rate or rhythm, presence or absence of valvular disease, condition of the myocardium and the arteries. It is to some of these that I wish to call your attention particularly today.

Myocardial Disease.—There is no doubt that blood-pressure tends to be decreased in dying hearts. There are notable exceptions to this rule. One occasionally sees cases with high systolic pressure and advanced myocardial disease in which the high pressure is maintained almost to the moment of death from cardiac failure.

It is surprising how little well-controlled data one is able to find in the literature as to the effect of chronic myocardial disease on blood-pressure. If we turn to the two most authoritative up-to-date books on blood-pressure, those of Gallavardin and G. W. Norris, we find the following observations. Gallavardin states that in the course of chronic myocardial disease arterial tension is often a little elevated, without doubt on account of concomitant arterial or renal influences. Norris finds

that the pressure is variable, although, with the exception of the terminal stages, an increase will usually be found, the pulse pressure is often small, and that not infrequently myocardial cases show a normal systolic but a high diastolic pressure.

In the effort to accumulate data on the effect of myocardial disease and particularly myocardial failure on blood-pressure I have reviewed the cases of myocardial disease admitted to the University Hospital during the past ten years. The group selected for analysis included only cases with evidences of marked decompensation on admission and recovery of compensation at the time of discharge. In all these cases frequent determinations of blood-pressure were made. Cases were excluded if arhythmia was present (except occasional extrasystoles) if there was any marked change in pulse-rate or evidence of renal disease. A series of 20 cases was collected which seemed to offer a fair basis for comparison. All of these patients received drug treatment during at least part of their stay in hospital (the drug usually being digitalis) and some had courses of hydrotherapy.

In Table I, I have noted the first blood-pressure estimations in these 20 cases after admission and the last before discharge, and the differences between these figures. It will be noted that after improvement had occurred 11 cases showed no marked changes in systolic pressure, while in 4 there was a significant rise, and in 5 a significant fall. All the cases showing significant rises had a fairly low initial pressure, while all but 1 showing a fall had high initial pressures. These figures suggest that as cardiac function improves the systolic pressure may rise, fall, or remain stationary, but that whatever changes occur, tend to be in the direction of the normal.

In the case of diastolic pressure the trend in blood-pressure as the patients improved was decidedly downward. In 14 cases the diastolic pressure fell 10 points or more (in 10 cases 20 points or more), while in only 1 did it rise as much as 10 points.

The changes in systolic and diastolic pressures were, of course, reflected in the pulse pressures, which showed a decided tendency

TABLE I

BLOOD-PRESSURE DETERMINATIONS MADE DURING DECOMPENSATION IN CHRONIC MYOCARDIAL DISEASE AND AFTER RECOVERY OF COMPENSATION

No.	During decompensation.			After improvement.			Difference.		
	Systolic.	Diastolic.	Pulse-pressure.	Systolic.	Diastolic.	Pulse-pressure.	Systolic.	Diastolic.	Pulse-pressure.
1	122	94	28	145	98	47	+23	+4	+19
2	137	105	32	135	78	57	−2	−27	+25
3	155	120	35	135	70	65	−20	−50	+30
4	95	83	12	94	55	39	−1	−28	+27
5	130	90	40	98	73	25	−32	−17	−15
6	100	75	25	115	80	35	+15	+5	+10
7	170	140	30	152	115	37	−18	−25	+7
8	154	110	44	152	90	62	−2	−20	+18
9	165	110	55	160	100	60	−5	−10	+5
10	170	100	70	165	80	85	−5	−20	+15
11	200	150	50	200	90	110	....	−60	+60
12	120	65	55	115	70	45	−5	+5	−10
13	120	95	25	124	88	36	+4	−7	+11
14	160	100	60	135	82	53	−25	−18	−7
15	95	70	25	105	65	40	+10	−5	+15
16	110	80	30	108	65	43	−2	−15	+13
17	182	120	62	140	90	50	−42	−30	−12
18	175	90	85	175	70	105	....	−20	+20
19	110	50	60	130	60	70	+20	+10	+10
20	170	120	50	170	100	70	....	−20	+20

to increase. In but 3 cases did pulse pressure show significant decrease.

In angina pectoris the blood-pressure may be normal, increased, or slightly below the normal. Some of the cases without hypertension during the intervals between attacks may show high pressure in attacks, while others show no alteration in pressure whatever.

Riesman, in a recent paper before the Philadelphia County Medical Society, has emphasized the tremendous fall in pressure that may occur in coronary thrombosis. This drop in pressure is not strange in view of the terrific handicap imposed on the heart by the occlusion of a coronary branch of any size.

The widely held opinion that low blood-pressure is frequently the result of chronic myocardial disease has never been clearly demonstrated except in the case of advanced heart fail-

ure, although the two conditions are associated in some cases. I wish to exclude from the discussion here sudden or temporary hypotension, which may arise in a variety of acute conditions, including acute heart failure, especially heart failure in acute infections. In hypotension of long standing and without obvious heart disease we should never be willing to attribute the hypotension to cardiac weakness without proof of deficiency of cardiac function. It is much more likely that the low pressure will be found due to some other cause if carefully looked for.

I should like to call your attention particularly to two types of hypotension which are sometimes mistakenly regarded as of cardiac origin. The first of these is due to undernutrition and the second is probably congenital. Our records show extreme instances of low blood-pressure due simply to undernutrition. A case in point was seen recently in a patient who, on account of gastric neurosis associated with constipation, had become extremely emaciated. At that time his blood-pressure was 85–65 mm. With no other treatment than diet and measures designed to relieve constipation he gained 22 pounds in six weeks and the blood-pressure rose to 110–70 mm. In the congenital group we have recently seen 2 strikingly similar cases in physicians, 1 fifty years old and the other just under forty. Both had been exceptionally fine athletes in their college days, and both, so far as can be determined, are in excellent health at present, with unusually good tolerance to physical exertion. Yet in these men, one weighing 220 and the other 170, systolic blood-pressure for many years has ranged between 95 and 105 mm.

Much attention has been paid to the study of blood-pressure changes that occur as a result of exercise, and a number of so-called tests of cardiac function are based on such data. In the normal person systolic pressure increases and diastolic pressure falls as a result of exertion sufficient to require definitely increased cardiac output. Immediately after the cessation of exercise there is a sharp drop in systolic pressure, then a secondary rise, and finally a return to normal. That changes from the usual curves of pressure may occur if the myocardium is inade-

quate is undeniable. But how far we may go in interpreting such results as a measure of cardiac function is not yet established.

Valvular Diseases.—With the striking alterations in arterial blood-pressure and pulse occurring in free aortic regurgitation you are all familiar. But the high systolic and low diastolic pressures, water-hammer pulse, Traube and Durosiez signs, and capillary pulse all may occur at times in forms of vascular erethism without aortic regurgitation, notably hyperthyroidism. Gallavardin states that similar blood-pressure figures may be found in cases with arteriovenous aneurysms or in patulous ductus botalli. There may be a wide pulse-pressure in certain cases of arteriosclerosis, but in my experience not an extremely low diastolic pressure. Nevertheless, in every case showing the vascular signs mentioned above, aortic regurgitation should be carefully looked for.

It should be emphasized that not all cases of aortic regurgitation show the characteristic vascular signs. There seems to be some relationship between the degree of regurgitation and the alteration in blood-pressure. That the latter is due largely to peripheral vasomotor influences cannot be denied, but in the last analysis the vasomotor changes are secondary to the regurgitation. At all events, slight grades of regurgitation, notably those occurring in simple sclerosis of the valves, are usually accompanied by smaller changes in blood-pressure and less characteristic pulse phenomena. But in nearly all cases there tends to be at least slight increase in pulse-pressure over the normal.

The statement is often made that in aortic regurgitation blood-pressure is much higher in the femoral artery than in the brachial, and this sign has been accredited with diagnostic value. In normal persons the pressure tends to be somewhat higher in the femoral, and this, according to Starling, is due to the greater rigidity of the femoral and the more localized peripheral resistance, causing large reflected waves which are summated on the advancing waves. This is said to be able to bring about a pressure in the femoral even higher than that of the aorta. Recent clinical investigations have shown that not only is a great increase in femoral pressure over the brachial found in aortic regurgita-

tion but also in certain cases of hyperthyroidism (Dr. Sailer has pointed out this) and arteriosclerosis. Moreover, there has been shown to be a large minority of cases with aortic regurgitation in whom the great differences in pressure are absent. Whether or not the explanation offered by Starling is adequate to account for the large differences in pressure found in these pathologic states, or whether some of the other factors suggested are of importance, has never been demonstrated. It has been found that in some cases the great difference in pressure disappears if the leg is plunged in hot water, while in others it is abolished by repeated compression and decompression of the femoral. From the clinical side the most important thing for us to remember is that the test has no very great value in the diagnosis of aortic regurgitation and even less in estimating the extent of the valvular lesion.

When in addition to aortic regurgitation there is coincident stenosis, the blood-pressures tend to be more nearly normal, *i. e.*, the systolic pressure is not so high as in pure regurgitation, and the diastolic, higher. In cases of extreme aortic stenosis and not much evidence of regurgitation the systolic pressure may be low and the pulse-pressure small. Some writers claim that the relative grades of regurgitation and stenosis may be gaged from the blood-pressure readings.

In the course of cardiovascular examinations in an army cantonment, where we accumulated a great deal of data on blood-pressure in well-compensated cases of mitral stenosis and mitral regurgitation, the evidence appeared to show that there was strikingly little if any alteration from the normal. Norris states that in compensated mitral insufficiency arterial pressure is practically normal, and in compensated mitral obstruction pressure is, owing to peripheral vasoconstriction, more often above than below the normal, and that the pulse-pressure is small.

In the attempt to analyze blood-pressure findings in the cases of mitral valvulitis admitted to the University Hospital great difficulty was encountered. These patients nearly all were decompensated, and it was hoped that such a group might be

compared with the cases of myocardial disease and decompensation, but without valvular disease, collected in Table I. Certain points quickly became apparent. Nearly all cases of mitral stenosis had also evidence of associated regurgitation. More than half the cases had profound disturbances of cardiac mechanism, of which auricular fibrillation occurred most frequently. Many of the other cases had to be excluded on account of disturbing factors, such as adherent pericardium, renal disease, aortic valvulitis, active infection, and other less frequently found conditions. It is impossible to draw definite conclusions from such material as we were able to collect, but in the cases apparently without complications other than myocardial disease and decompensation, some showed normal pressures, while in others there was decided lowering of the systolic pressure. Decreased pulse-pressure was the most frequently found abnormality.

In combinations of aortic regurgitation and mitral valve disease (a frequent association) the aortic lesion usually dominated the clinical picture and the vascular signs were those of aortic regurgitation. The systolic pressure, however, did not tend to be as high as in uncomplicated aortic regurgitation. In some cases in which the mitral disease appeared to be prominent and the aortic regurgitation slight the peripheral pulse signs of the latter condition were lacking, but in practically all such cases there was some increase in the pulse-pressure.

Pulse-rate.—Von Recklinghausen showed a number of years ago that pulse-pressure varies directly with output of the heart per beat except for difference due to the coefficients of elasticity of arteries. It has also been shown that output per beat is largely dependent on the heart rate. Consequently, other things being equal, one should expect to find a large pulse-pressure in bradycardia and a small pulse-pressure in tachyardia. But in patients there are always a number of factors that disturb theoretic considerations. In tachycardia one finds such things as lessened vagal inhibition and increased accelerator action, which not only have effects on the contraction of the heart, but a repercussion on the vasomotor apparatus. There is no doubt,

however, that alterations in pulse-rate tend to modify blood-pressures. In the case of tachycardia the direction of this modification is dependent somewhat on the cause of the tachycardia. In tachycardia due to exercise or hyperthyroidism systolic pressure is usually increased and diastolic pressure decreased. In the tachycardias resulting from infection, systolic pressure, if altered, is usually decreased. In tachycardia of nervous origin both systolic and diastolic pressures tend to be increased and may be greatly elevated.

In bradycardia due to overaction of the vagus, especially sudden attacks of vagus inhibition, blood-pressure, both systolic and diastolic, is decreased and may be very low, The vagal attacks are usually transient, passing off quickly. In bradycardia from whatever cause diastolic pressure is usually lowered and the pulse-pressure increased. Systolic pressure is variable. Gallavardin, in calling attention to the low diastolic pressure of bradycardia, has designated it "diastolic pseudohypotension." This low pressure is doubtless due largely to the continued outflow of blood from the arteries during the long diastole. Gallavardin has, therefore, suggested that true diastolic hypotension is to be differentiated from pseudohypotension by the abruptness of the descent from maximum to minimum pressure rather than the actual minimum pressure attained.

Abnormal Cardiac Mechanisms.—The blood-pressure is affected more or less profoundly by all types of cardiac arhythmia. Part of this change in pressure may be attributed to lessened mechanical efficiency of the cardiac pump when the muscle contracts in an abnormal manner, and part to alteration in length of cardiac cycles, which influence ventricular filling and contractile power of the muscle.

In sinus arhythmia, the pressure tends to be slightly lower during the time the cardiac action is more rapid, and higher when the action is slowed. In slight grades of respiratory arhythmia the pressure changes may be so small as to escape observation, but in more marked cases systolic pressure may be 10 to 20 mm. higher during expiration (the period during which the rate slows) than in inspiration.

In extrasystolic arhythmia the pulse corresponding to the premature beat is practically always weaker and the succeeding beat of normal type stronger than that of successive normal beats. The blood-pressure should, of course, be estimated during periods of normal rhythm, and usually extrasystoles occur infrequently enough that there is no difficulty in this respect. In some cases, however, extrasystoles occur so frequently and at such irregular intervals that the blood-pressure variations resemble those of auricular fibrillation, and methods applicable for measuring pressure in fibrillation are in order. In pulsus bigeminus the effect of the abnormal rhythm is to increase the systolic and lower the diastolic pressures of the beats of normal type. The more ineffective the premature beats, the greater these changes are likely to be.

In complete heart-block alterations in pressure are somewhat similar to those found in simple bradycardia. In cases with extremely slow ventricular rate (30 or less) diastolic hypotension is usually quite marked. Systolic pressure is elevated in a large percentage of cases, but not invariably so. A case with slight aortic regurgitation recently in the wards, on suddenly developing complete heart-block with a rate of approximately 30 (the rate previously having ranged from 70 to 80), had a fall in systolic pressure from 130 to 120 and a fall in diastolic pressure from 60 to 50 mm. Two days later, the block continuing, the pressure was 140–50 mm.

In complete heart-block, and particularly in those cases in which there are transitions into and out of complete block, the condition of ventricular standstill may develop for a number of seconds or there may be a series of ineffectual beats. Under such circumstances the blood-pressure doubtless sinks very low, and the seizures known as Stokes-Adams' syndrome occur.

In paroxysmal tachycardia the characteristic alterations in pressure accompanying the paroxysms are definite fall in systolic pressure and decrease in pulse-pressure. The diastolic pressure may be either increased or decreased. A very instructive study of a case was recently reported by Barcroft, Bock, and Roughton. With the onset of a paroxysm of tachycardia the minute vol-

ume of blood flow dropped from 5–6.1 to 2.8–2.1 liters per minute, the systolic output from 77.5 to 12.9 c.c. per beat, the systolic blood-pressure dropped from 120 to 100, but the diastolic pressure rose from 68–70 to 80. In this case the fall in pulse-pressure, as might be expected from the tremendous drop in output per beat, showed the most conspicuous alteration of all the pressure changes.

Auricular fibrillation is characterized by irregular irregularity in the force and frequency of the pulse. Consequently, the blood-pressure of successive beats may show very wide variations, and accurate determinations of pressure cannot be made with available clinical methods. James and Hart have devised a method in which "average systolic pressure" is calculated by data obtained from counting the heart rate and the number of beats that come through to the radial with various pressures exerted by the cuff on the upper arm. Lundsgaard and Cohn have proposed a modification of the old Gärtner tonometer method of estimating blood-pressure in the digital arteries as a more accurate method than that of James and Hart. The principle of the Gärtner method is to make the finger bloodless and observe at what level of constricting pressure a flush returns to the finger distal to the constriction.

For routine clinical work the following method will be found as satisfactory as special methods: The ordinary auscultatory technic of determining pressure is used, and the levels at which beats begin to come through and at which most beats come through is noted. The pulse deficit is also counted. The diastolic pressures do not vary so greatly as the systolic pressures and can usually be approximated by the auscultatory method. In this way one is usually able to determine the presence of either definite hypertension or hypotension, and estimate the extent to which the heart is handicapped by ineffective beats. It should be remembered in this connection that the general level of pressure is usually lower during fibrillation than is to be expected in normal rhythm, although isolated beats may show pressures quite as high or even higher.

In pulsus alternans the blood-pressure is usually high, as

this condition occurs most frequently in cardiorenal disease. Exceptions to this rule are found in certain cases of myocardial disease with simple tachycardia, in paroxysmal tachycardia, in auricular flutter with rapid regular ventricular rate, and in occasional cases of digitalis intoxication. As a rule the differences in systolic pressure between the stronger and weaker beats is slight, but in pronounced cases may be as much as 20 mm. of mercury. The diastolic pressures may also alternate, but the variations are not as great as the systolic. Judging from sphygmograms, postextrasystolic pulsus alternans shows transiently the same type of alteration in pressure as continuous alternation, but it rapidly diminishes, and after a variable number of beats disappears.

Clinically, pulsus alternans may be regarded as one of the types of response of weakened or diseased heart muscle to overstrain. If tension is lowered or rate decreased, alternation is lessened and may entirely disappear.

Pericarditis.—In pericardial effusion systolic pressure tends to be lowered and pulse-pressure decreased. The greater the effusion or the more rapid its development, the more profound the changes in pressure. The pressure of pericardial fluid interferes with ventricular filling, and from this cause may seriously embarrass the circulation and even result in death. In extensive pericardial adhesions which mechanically cripple the cardiac movements there may be lowering of systolic pressure and lessening of pulse-pressure similar to that seen in pericardial effusion. However, in many cases, particularly those arising in pancarditis of childhood, the influence of adherent pericardium on blood-pressure is masked by associated aortic regurgitation.

The so-called pulsus paradoxus or marked weakening of the pulse during inspiration occurs in some cases of adherent pericardium or pericardial effusion. According to Sahli it is of value in the diagnosis in adherent pericardium only when there is concomitant inspiratory engorgement of the jugular veins, a symptom which indicates a stenosis of the jugular veins during inspiration.

Relation of the Heart to Blood-pressure in Nephritic Hypertension.—The cause of nephritic hypertension is still one of the

unexplained phenomena of disease. It seems, however, to be pretty well established that it is at least in part an adaptive process for the renal defect. The heart, being forced to pump against the increased pressure, undergoes muscular hypertrophy and dilatation of the chambers in order to increase its efficiency. But the increase in cardiac power is eventually limited by the involvement of its blood-supply in the universal vascular disease. The increased cardiac work demanded appears to be purely compensatory, as it is expended in maintaining the high level of pressure, while the rate of the circulation remains little changed. Experiments have shown that even with marked hypertension, minute volume of blood flow and systolic output per beat remain practically unchanged or are diminished.

In a large proportion of cases of nephritic hypertension the terminal events are due to cardiac failure, and it is instructive to observe the behavior of the blood-pressure in such cases. One finds that even with obvious failure of the heart and advanced passive congestion the high pressure tends to be fairly well sustained. There is often slight or moderate fall, affecting the systolic pressure more than the diastolic, thus bringing about decrease in pulse-pressure. Large drops in pressure rarely occur until the heart approaches complete exhaustion. Moreover, it is not unusual to find increasing heart failure associated with increasing hypertension, the failure being hastened, no doubt, by the increased burden of work.

The most striking fact revealed from the study of blood-pressure curves in cardiorenal disease is the tenacity with which the circulatory mechanism is held to the maintenance of hypertension in spite of clear evidences of heart failure. This is one of the indications of what compelling influences to work may be brought to bear on the heart, and suggests to what an extent adaptive measures may be called into play to combat handicaps imposed by disease.

Treatment.—I do not wish to discuss treatment in detail here, but will merely invite your attention to a few principles. To treat intelligently the conditions in which abnormal blood-pressures are present it is first necessary for us to realize that

high or low pressure is not a disease, but a sign of disturbance in function of some part of the body mechanism. If the alterations in pressure are due to heart disease, it is quite obvious that if treatment is indicated, it should be directed toward improvement of the cardiac function. It should be equally obvious that if the heart is not responsible for abnormal pressure, nothing worth while is to be gained by treatment of that organ. The fact that so-called cardiac stimulation in surgical shock is futile is now fairly well appreciated, but it should be equally appreciated that patients with chronic hypotension not of cardiac origin are more effectively treated by combating the cause than by merely giving them digitalis. The case I have cited in which pressure rose from 85–65 to 110–70 coincidently with recovery of nutrition is one of many instances that might be quoted.

We do not often attempt to alter the very abnormal pressures found in free aortic regurgitation, since we have been taught that these alterations in pressure are due largely to the action of the mechanisms compensating for the cardiac deficiency. But frequently one sees nephritic hypertension treated drastically and with serious consequences. It is not recognized sufficiently that the high level of pressure may be necessary to keep the kidneys at work.

On the other hand, it must be recognized that extremely high or low pressures are of themselves liable to be of serious consequences. For example, a patient with marked hypertension is expected to succumb either sooner or later to the consequences of renal deficiency, cardiac failure, or apoplexy. The proper treatment of such a case depends not only on the recognition of the cause of the hypertension, but wherein the chief danger lies.

All this brings us back to the well-established principle that the greater part of treatment is accurate diagnosis. If we adhere to this, we are liable to do our patients little harm from meddlesome treatment even if we are unable to afford them relief, and we establish ourselves on the only foundation from which improvement in therapy may be hoped for.

CLINIC OF DR. TRUMAN G. SCHNABEL

GASTRO-INTESTINAL CLINIC, OUT-PATIENT DEPARTMENT, UNIVERSITY HOSPITAL

SYPHILIS OF THE KIDNEY

ALTHOUGH syphilis enjoys the unusual distinction of having a satisfactory serologic test, a certain etiology, and a specific therapy, still there remain in connection with this disease many difficulties of a diagnostic and therapeutic character. We have one patient to show and the case history of another patient to review, illustrating such problems of diagnosis together with some interesting features in the matter of therapeusis. Both patients were admitted with predominant gastro-intestinal symptoms and were shown to have strongly positive Wassermann reactions. In the patient we have here today the important lesion is presumably luetic and extragastro-intestinal. In the other case the lesion was intragastric and, although it seemed possibly to be of syphilitic origin, proved at autopsy to be neoplastic.

Case No. 29,404 is a negro aged thirty-six; admitted September 6, 1922. The chief complaints date back one year prior to admission, with the history of abdominal pain, "gas on the stomach," constipation, and a sense of choking. The attacks of abdominal pain were variable in time and nature, becoming more intense during the last weeks before admission. The pains usually followed immediately after food intake and were not influenced by bicarbonate of soda. There was some nausea and vomiting throughout the entire year. There was a decided cathartic habit. The choking sensation was quite uncertain in type; apparently it was not a globus. There was no difficulty in swallowing and the appetite was good. There

were no pronounced cardiorespiratory symptoms, although there was some evening swelling of the feet. There was a regular nocturia of one urination. A loss of 11 pounds in weight was reported.

The patient had typhoid fever, but denied any genital or other skin lesions. The family and social history are practically negative. He has a living child and his wife has had no miscarriages.

On physical examination the outstanding features were rather markedly palpable peripheral arteries with no unusually palpable peripheral glands. The blood-pressure was 120 mm. systolic and 85 mm. diastolic. The patellar jerks were only obtained on reinforcement. There were no unusual skin sensory changes. The pupillary reflexes were normal. There was a rather marked amount of dental caries and some pyorrhea. Some of the teeth were gold capped. Examination of the chest and abdomen was practically negative. There was no edema in the extremities and there was no unusual roughening of the tibiæ.

With this much evidence tentative diagnoses of constipation, vascular sclerosis, dental caries, and oral infection were made. The gastric symptomatology was regarded as a secondary manifestation. Medication, which included sodium bromid and cascara sagrada, with directions for a bland diet, yielded a very good report at the time of his second visit. He was free of abdominal pains and the choking was better.

On this date, after an Ewald-Boas meal, 70 c.c. of the gastric contents were withdrawn at the end of one hour. The free hydrocloric acid titration showed 20 c.c., while the total acidity showed 40 c.c. in terms of decinormal sodium hydroxid solution. Occult blood was negative. The contents were negative microscopically. Gastric inflation through the ordinary Einhorn type of duodenal tube showed the stomach to be in good position. This inflation maneuver is quite accurate in determining the size and position of the stomach. It is an old but very good method. One listens over the abdomen while air is gently forced into the stomach by means of an ordinary inflation bulb, such

as is used on a sphygmomanometer cuff or a hand atomizer. When the bell of the stethoscope is placed over any portion of the stomach the air entering the stomach through the tube produces a cavernous sound either whistling in character, if the stomach is empty, or of a bubbling nature, if fluid remains. Always determine the size and position of the stomach in this way after the test-meal has been removed. Efforts in this direction result in findings which compare favorably with the *x*-ray gastric shadow obtained in the same case.

The first specimen of urine was obtained at the time of this second visit when, much to our surprise, a very heavy cloud of albumin was demonstrated. The specific gravity of the urine was 1020 and there were numerous hyaline and granular casts in the centrifuged specimen. We made no search for the double refractile lipoids. At this visit the patient was placed on a régime calculated to influence a chronic nephritis.

During the course of the following three weeks very little change was noted in the patient's condition. He continued somewhat better from the gastro-intestinal standpoint, but there remained the choking sensation in the throat. The urine continued with a heavy cloud of albumin, casts, and a specific gravity always over 1020. An *x*-ray of the chest was negative. There was no widened aortic or cardiac shadow. The blood Wassermann was returned strongly positive on the sixth visit. On the seventh visit the patient again complained bitterly of his abdominal pains and he had been vomiting. He now was voiding urine three to four times at night. He was on this date referred for intravenous arsphenamin therapy.

Since that time he has received three injections of this drug, and after the second treatment was entirely free of symptoms. The urine contained only a minute trace of albumin and no casts. After a third injection there continued only the very faintest trace of albumin in the urine. Today the phenolsulphonephthalein test yielded 25 per cent. for the first hour and 20 per cent. for the second hour.

Here, then, we are probably dealing with a patient having syphilis of the kidneys. The diagnosis is only presumptive,

as such diagnoses usually are. Unfortunately, we failed to sense the true state of affairs until it was too late to try any of the renal functional tests. One of the clinical clerks on the occasion of this patient's first visit suggested the additional diagnosis of neurasthenia. To this suggestion was made the comment that the patient had none of the earmarks of a functional case, and that the diagnoses already made adequately explained the original symptoms. Whether or not this patient had or has renal syphilis, the case serves to emphasize the importance of an early complete investigation of every case from every standpoint. It is a poor plan to view a single organ in isolation from the rest of the body. It is also an extremely dangerous plan to make the diagnosis of neurasthenia even after repeated visits of the patient and thorough study. This seems bromidian, yet it needs a daily emphasis. Always make a diagnosis at the time of the first visit; it may be incorrect, but subsequent visits will permit of a revision. Many cases become more and more difficult to diagnose if we postpone a definite opinion in black and white.

Syphilis of the kidneys receives little attention in the literature. It probably is a rare lesion, but, in all likelihood, occurs more frequently than we suppose. Authorities differ as to the incidence of this lesion. Usually the diagnosis is made on the strength of the effect of antiluetic treatment. If the urinary evidence improves on this régime then it is reasonably certain to assume the diagnosis. We shall again refer to the method of making a syphilitic diagnosis by therapeutic test. Great caution must be taken not to mistake the urinary findings that may appear in syphilitics, after intensive mercurial treatment. The albumin casts and blood that may occur under such a plan of treatment usually clear up when mercury is discontinued. In luetic nephritis this does not happen.

To begin with, we must not forget that the syphilitic may have a non-specific nephritis. Nevertheless, just as in other infectious diseases, so in the primary and secondary stages of syphilis, we may have a transient albuminuria or the more severe grades of acute nephritis which are spirochetal in origin.

Clinically such a picture cannot be easily differentiated from that due to other causes. Usually one finds greater amounts of albumin, and for some reason or other these patients do not seem as sick as certain features of the case would indicate. The spirochetes have been obtained in ureterally catheterized urines. Pathologically, the kidneys differ in no respect from those obtained under different circumstances. The spirochetes have also been demonstrated in the kidneys of acute syphilitic nephritis.

Double refractive lipoids are found abundantly in the urines of these nephritic patients, as pointed out by Munk in 1913. Drs. Stengel and Austin, in our hospital, showed in 1915 that these bodies may be found in degenerative nephritic urines other than those having a syphilitic etiology. These lipoid drops when viewed with a polariscope appear to have a dark cross separating four white quadrants. In 1921 two residents in our hospital examined the urines of 50 syphilitics without manifest true nephritis. The Drs. Taylor who did this work found no double refractile lipoids in these urines. A great abundance of these refractile bodies is suggestive of a syphilitic nephritis in the presence of marked urinary symptoms and a positive Wassermann. It requires, however, a successful therapeutic effort to finally establish the diagnosis clinically.

The late nephritic lesions in syphilis include gumma and amyloid kidney as well as the usual grades of chronic nephritis. Our case probably has a predominantly tubular involvement. The difficulties of diagnosis apply here as they do in the acute variety, and the same diagnostic criteria hold; viz., The proof of a luetic infection, the symptoms of nephritis usually with a high albumin content in the urine, the presence of spirochetes in the catheterized urine, and the favorable influence of a specific therapy. Pathologically as well as symptomatically there is nothing to definitely distinguish these chronic nephritis cases from others of non-syphilitic origin.

Our own case, with its very marked therapeutic results, duplicates the usual experience met with in chronic cases. Arsphenamin intravenously is the drug of choice over against

mercury. Small doses (0.1 to 0.2 gm.) should be tried out, and repeated examinations of the urine should be made in order to determine any harmful effects the drug may have. Usually improvement comes quite promptly if the lesion is luetic.

CARCINOMA OF THE STOMACH IN ASSOCIATION WITH A POSITIVE BLOOD WASSERMANN AND THE HISTORY OF CHANCRE

CASE history No. 25,372 pertains to a mulatto aged forty-three. He was admitted June 28, 1920, with a history of "stomach trouble." There was complaint of nausea and vomiting following very soon after meals, with a dragging pain to the left of the umbilicus. He weighed on admission 132 pounds; his average weight had been about 173 pounds.

On examination the patient proved to be a somewhat emaciated individual with signs of an extensive fibrosis throughout the right lung. The heart was on the right side. There was some rigidity of the right rectus, with a vague mass in the right epigastrium. There was some visible peristalsis in the upper left abdomen. Test-meal studies showed at least a twenty-four-hour retention, with no free hydrochloric acid or pepsin present in the gastric contents. The occult blood reaction was positive.

It seemed quite certain that we were dealing with an organic pyloric obstruction, and we therefore referred the patient to the hospital wards for further study and a subsequent operative procedure. He gave a history of having had a chancre at the age of fifteen. He is credited in another institution in this city with nine admissions. In 1913 and 1915 the diagnoses made in this other hospital were chronic gastritis. At these times he experienced severe abdominal attacks of pain lasting many weeks. There was a diagnosis of pulmonary syphilis made on one of his admissions, and the remaining times either chronic alcoholism or delirium tremens were noted. In our medical wards the blood Wassermann was returned strongly positive and the *x*-ray showed a filling deficiency in the immediate pyloric region with a forty-eight-hour bismuth meal retention. The surgical opinion was adverse to operation.

In view of the positive Wassermann it was suggested that antiluetic treatment be tried. During the course of the next two months he received six intravenous injections of arsphenamin. At the end of this time he did not vomit, felt better, and returned to work. His anemia improved somewhat and he maintained his weight. After this series of injections the *x*-ray showed a thirty-hour retention and the pyloric region filled out satisfactorily. In other words, it seemed both objectively and subjectively that he was improving. There occurred then some difficulty with one of the hospital authorities, and he disappeared. We have learned since that he died in January, 1922 in another hospital. At autopsy among other findings there was found an adenocarcinoma of the stomach.

Although it was confidently believed that this case was neoplastic, still the temporary improvement on antiluetic treatment made it seem that we might be dealing with a syphilitic gastric lesion. Sometimes new growths seem to improve in this way when subjected to specific therapeusis. Those dealing with epithelioma about the head at times report marked improvement on mercury and arsphenamin when the patient presents a positive serologic test for syphilis. This, of course, suggests that we cannot always be sure of a lesion as being spirochetal even though it improves on treatment, and, conversely, there are times when syphilitic lesions fail to respond to treatment—this is true when the pathology is well advanced, usually visceral and tertiary in time. Carcinoma and syphilis may occur as separate lesions in the same individual. It is usually a good plan to explain as many of a patient's symptoms on as simple an etiology as possible, and often syphilis answers the diagnostic question completely. Sometimes, however, it is only a coincident diagnosis. This must be continually kept in mind.

Syphilis of the stomach in common with that of the kidney or, indeed, of any viscus is often difficult to diagnose. Clinically, there is no characteristic picture for such a gastric lesion. The diagnosis usually is made on the evidence of syphilis elsewhere in the body, on a positive Wassermann reaction, on *x*-ray find-

ings, and on the effect of antiluetic treatment. It is rather interesting that the diagnosis is rarely made in this community. It can scarcely be that we overlook the lesion when it is such a uniform experience. Naturally, certain conditions are more frequently found when one is on the lookout for them. The matter of gastric syphilis is receiving an increasing amount of attention from all sides. One series of 38 cases has been reported and others of lesser number. We rather believe that the condition is less common here than elsewhere, although this would be difficult to prove.

The lesions occur during the secondary and tertiary stages. Usually we meet with the most pronounced changes during the tertiary stage. At this time we may find simple ulceration, gumma, or a diffuse involvement of the entire gastric wall, simulating the better known leather-bottle type of stomach seen in carcinoma. Frequently the gummas break down, when we may have large, ulcerating tumor masses. We find here, as in other parts of the body, the characteristic, round-cell infiltration of syphilitic invasion. We may, of course, have extragastric syphilis invading the stomach by continuity, and rarely a diffuse lesion involving the pylorus, with resulting obstruction.

The history of these gastric syphilitics is usually atypical. The acid values vary. Some writers report a low acid content, while others report little change in the free and total acidity. All manner of changes are observed by *x*-ray examination, but there is nothing characteristic of the disease. Sometimes in stomach syphilis one finds unusual filling defects which have the earmarks of carcinoma. These patients usually do not have the emaciation, anemia, and other symptoms common in those having neoplasms of like stage. The Wassermann is of incalculable help. It should be done for all chronic gastric cases. It must be cautioned, however, that not all gastric cases with a positive Wassermann are syphilis of the stomach. Many syphilitics have stomach complaints, and it has been shown recently by Stokes and Brown that a large percentage of such cases have neurosyphilis. The same authors re-emphasize the great

diagnostic value of spinal fluid examination over against and with the blood Wassermann.

The treatment of a real case of gastric syphilis indicates the use of arsphenamin and mercury in the usual way. If, of course, we are dealing with gastric symptomatology in a

Fig. 142.—Sphygmomanometer cuff with long rubber tube and rubber inflation bulb.

neurosyphilitic the attention must be directed toward the nervous system. Sometimes healed syphilitic lesions of the stomach require operative interference because of consequential deformities. If the problem of operable neoplasm of the stomach arises, then we should do a laparotomy before the therapeutic

test for syphilis is carried out. If, as in our case, the lesion is inoperable, then treatment for syphilis should precede an operation.

We have another case in whom we suspect a luetic infection. Before one of you obtains this patient's blood we wish to call

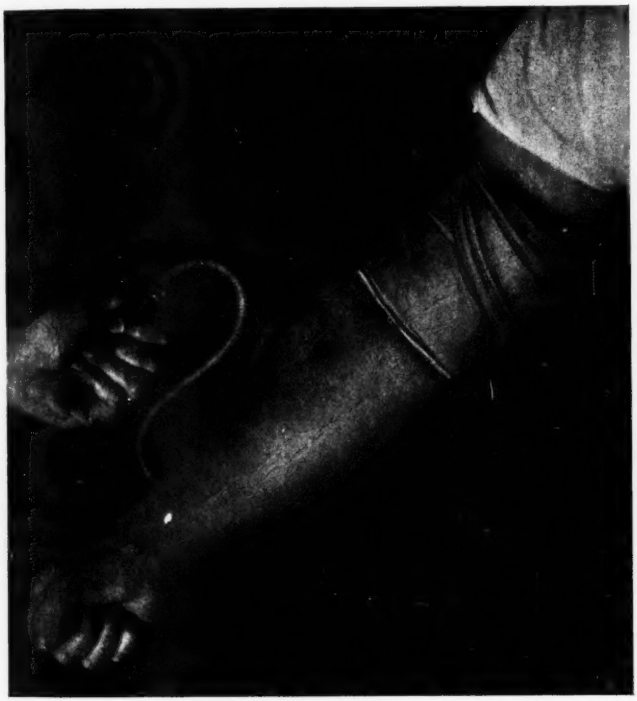

Fig. 143.—Sphygmomanometer cuff applied to arm.

attention to the use of the sphygmomanometer cuff as a tourniquet in obtaining blood for the Wassermann test. The need for a tourniquet has increased immeasurably with the frequent practice of intravenous therapy, transfusions of various types, and blood withdrawal from the median basilic or cephalic veins for diagnostic purposes. For a long time we have found the use of

the sphygmomanometer cuff during venipuncture by far the most convenient device for arm constriction. Hoge originally suggested its use in this way, and we believe that its availability for this purpose should be more generally known. With this sphygmomanometer attached, the operator is in a position to carefully observe the amount of pressure exerted, and is able to increase or to relieve the pressure at the proper moment. No assistant is needed to control this tourniquet and, therefore, there is less chance for mishaps to occur. Occasionally an untrained assistant, in an effort to release other tourniquets, disturbs the position of the arm so that the intravenous needle may be wholly or partially pulled out of the vein.

In the course of tranfusion, however, the sphygmomanometer itself is frequently in the way of the operator; so that it was thought advisable for tourniquet purposes to use a sphygmomanometer cuff without the sphygmomanometer. A cuff is used with but a single outlet to which is attached a rather long rubber tube; to the other end of this tube is attached a rubber inflation bulb with a fine screw adjustment to control the outlet of air. With this scheme correct constriction can be conveniently maintained just below the systolic pressure point. This is important in the arm of the blood donor. Further than this, the constriction can be accomplished at the necessary time and in the minimum amount of time without disarranging sterile dressings or moving the patient's arm. The rubber inflation bulb is brought out from underneath the sterile coverings and is placed in a position easy for the operator to reach. Sphygmomanometer cuffs are now available in all hospitals and doctor's equipments. They are as conveniently to be had as bandages, rubber bands, or other devices ordinarily used as tourniquets.

SUMMARY

1. Attention is called to the disease entity syphilis of the kidney, which includes transient albuminuria, acute and chronic nephritis, gumma, and amyloid disease. Most of these may be spirochetal in origin, and usually present no distinctive clinical and pathologic picture.

2. The diagnosis of syphilis of the kidney is made on the strength of the (1) history of a luetic infection, (2) evidences of syphilis elsewhere in the body, (3) a positive Wassermann, (4) abundant presence of the double refractile lipoids in the urine, (5) the evidences of a true nephritis, especially the finding of a large amount of albumin, (6) spirochetes in the catheterized urine, and (7) the favorable influence of antiluetic infection.

3. Arsphenamin is the drug of choice; initial small doses should be used.

4. A case history of gastric carcinoma with chancre and a positive Wassermann is presented to serve as a text for the brief exposition of the topic of gastric syphilis.

5. Attention is called to the increasing interest being manifested in syphilis of the stomach, including simple gastritis, ulcer, gumma, and diffuse infiltrative lesions of the gastric wall.

6. No distinctive clinical picture is possible for these lesions unless it be in those instances of unusually extensive bismuth shadow deformities in a patient who has few of the evidences found in those having well-advanced neoplastic invasion of the stomach.

7. Diagnosis of gastric syphilis depends on the (1) presence of syphilitic lesions elsewhere in the body with the history of a primary lesion and a positive blood Wassermann, (2) the evidence of stomach lesions by *x*-ray study, and (3) on the successful exhibition of antiluetic treatment.

8. Points are made for the occasional fallibility of the therapeutic test in syphilis, as well as the occasional failure of antisyphilitic treatment in luetic patients.

9. Symptomatic improvement on treatment for syphilis does not always justify a diagnosis of visceral syphilis in a Wassermann positive case.

10. Therapeutic procedures are indicated in operable and inoperable gastric carcinoma with positive serologic evidence for lues.

11. Other points are made concerning (*a*) the importance

of early complete investigation of all chronic cases, especially the determination of the Wassermann reaction in blood and the investigation of the spinal fluid in syphilitics with gastric symptomatology.

(*b*) The advisability of postponing a functional diagnosis for a long period and only after every organic possibility has been eliminated. Sometimes it requires years to reverse a diagnosis of neurosis.

(*c*) The value of the combined inflation and auscultation method in determining the position of the stomach.

(*d*) The convenience and satisfaction to be experienced in using the sphygmomanometer cuff as an arm tourniquet.

CLINIC OF DR. CHEVALIER JACKSON

JEFFERSON HOSPITAL

BRONCHOSCOPIC CLINIC

LUNG SUPPURATION CAUSED BY PROLONGED SOJOURN OF FOREIGN BODY

WE have had at the Bronchoscopic Clinic over 200 cases of lung suppuration in which a foreign body was the cause. The foreign body had been present for periods varying from a few weeks to thirty-six years, and in a number of the cases the presence of a foreign body was unsuspected. One of the most striking things in these overlooked cases is the inevitable conclusion that countless thousands of patients with lung suppuration have in past years been buried without the foreign body origin ever having been suspected, and the further conclusion that many of the cases were supposed to have died of pulmonary tuberculosis. This is evidenced by the fact that in all the older text-books the statement was made that foreign body in the lung ended in "phthisis pulmonalis." They undoubtedly did, but it was a non-tuberculous lung suppuration. This was in the days before the discovery of the tubercle bacillus, and the diagnosis of foreign body was usually made either postmortem or by the recovery of the patient after coughing up a foreign body. Before the days of Roentgen-ray diagnosis there was some excuse for overlooking foreign bodies; yet foreign body cases are still coming to the clinic overlooked for many years by neglect of the practitioner to call in the aid of the roentgenologist in every acute and chronic case of pulmonary disease. Furthermore, most *recently aspirated* foreign bodies of considerable size will give unmistakable physical signs of bronchial obstruction that should lead at once to the suspicion of foreign body. After suppurative processes have supervened the physical signs differ in no way from

those of lung suppuration of other origin. No dependence whatever should be placed upon a negative history; but given a history of foreign body plus the signs of bronchial obstruction, we have an absolute indication for a diagnostic bronchoscopy. A Roentgen-ray examination should always be made whether there are signs of bronchial obstruction or not, and *x*-ray examination should always precede the bronchoscopy whether the foreign body in question be of a kind opaque to the ray or not. In fact, in cases of peanut kernel and similar radiotransparent foreign bodies the ray signs of obstructive emphysema discovered by Iglauer and developed and applied by Manges with a high degree of skill are absolutely diagnostic.

Case I (Fbdy. No. 788).—*Personal History.*—This man, aged twenty-eight years, when a private in the United States Army had pneumonia in 1916, in bed one month; appendicitis in 1918, requiring operation in May, 1919; gassed October, 1918 in Argonne, in infirmary twenty-four days; influenza in February, 1919, in bed ten days; measles in March, 1919, in bed one week.

Present Illness.—In December, 1918 had an acute pneumonia; under treatment fourteen days while at Verdun, France. Evacuated to Camp Hospital 41 at Is-sur-Tille, France. The symptoms at this time were cough and spitting of blood. Evacuated to Base Hospital No. 103 at Dijon, where a thorough examination was made, including Roentgen-ray study, by which an abscess of the lung was discovered. The patient was invalided home to United States. Repeated sputum examinations were negative for tubercle bacilli. On arrival at Fort Sam Houston, Texas, the diagnosis of lung abcess was confirmed and, in addition, the very faint shadow of a foreign body was discovered in the abscess cavity. The patient then recalled that in December, 1918, while scuffling with a comrade he missed a pencil cap that he had had in his mouth; but he did not know that he had "swallowed" it. He remembered having "looked everywhere" without being able to find the pencil cap. In the activities of the front he had forgotten the incident and neglected to mention it to the medical officers who subsequently examined him. Patient was trans-

ferred to the Walter Reed Hospital and brought to the Bronchoscopic Clinic, Philadelphia, for the removal of the foreign body by bronchoscopy.

The *symptoms* at the various stages were cough, expectoration of blood; later expectoration of foul sputum, pain in the lower left chest of a rather diffuse character. Later still the pains were sharp and shooting, and were made worse on deep breathing. The latter pains were relieved after the coughing up of pus.

Physical Examination.—Omitting the portions of the examination which revealed nothing abnormal, the following points were elicited: The thorax was large; the left side contracted and flattened. Expansion markedly limited over the whole left side. Percussion hyperresonant over the upper half of the left chest; flat over the lower left lobe. Breath sounds normal on the right; distant over the upper left chest; absent over the lower left chest. Snapping and crackling râles on inspiration over the lower left lobe. Suggestion of a friction-rub. The heart was displaced to the left. P. M. I. fifth left interspace, 2 cm. outside the left nipple line. Asthmatoid wheeze absent at mouth. Extremities: Marked clubbing of fingers and toes; no edema (Fig. 144).

Bronchoscopy.—The left inferior lobe bronchus was found to end in a tightly strictured fistula with a long web of cicatrical tissue across the lumen. Granulations were removed with forceps, the fistula was dilated, and the bronchoscope was gradually insinuated for a depth of 3 cm. from the proximal end of the strictured passage. A cavity filled with mushy granulations was found, and in it a small portion of the foreign body was discovered and removed. The foreign body was then manipulated until its proximal end came into view and was grasped with side-curved forceps, disengaged from its bed, and removed.

Postbronchoscopic Roentgen-ray examination, by Captain F. F. Borzell, M. C., U. S. A.: Roentgenogram made immediately after removal of the foreign body does not show presence of foreign body, but the left chest still shows a marked amount of inflammatory exudate.

Postbronchoscopic Condition.—No reaction followed bronchoscopy. Expansion still limited on the left side. Percussion still

Fig. 144.—Case I (Fbdy. No. 788). Reproduction of a photograph showing the emaciated hands, clubbed fingers, and incurved, "watch-crystal" nails of a soldier with pulmonary abscess due to foreign body. The hands became perfectly normal in a few months after cure of the abscess by per-oral bronchoscopic removal of the foreign body under local anesthesia.

hyperresonant over the upper left chest, with marked dulness below. Breath sounds very distant over both sides of the chest.

There are a few râles over the left lower lobe and the friction-rub is still present. General condition excellent. Patient was taken back to Walter Reed Hospital. Today he weighs over 200 pounds and is in perfect health.

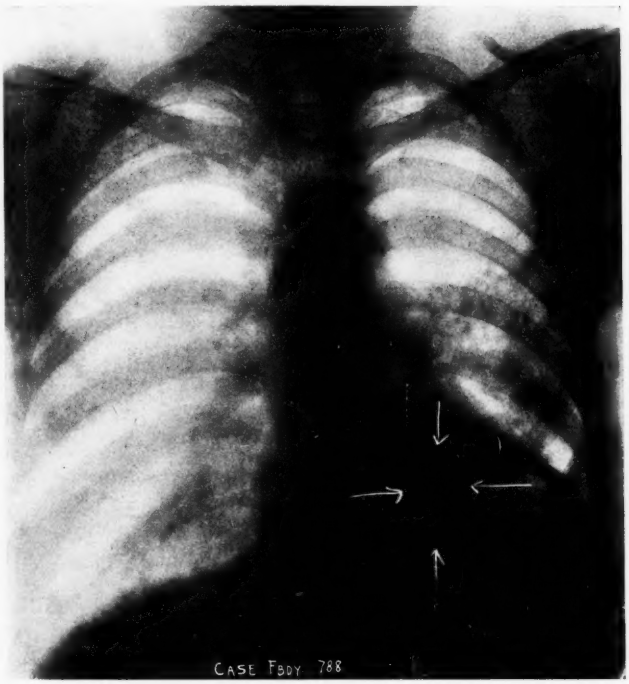

Fig. 145.—Case I (Fbdy. No. 788). Roentgenogram of a man aged twenty-eight years with abscess of the lung due to foreign body. Notwithstanding the foreign body is metallic it could not be made to show through the heart and abscess shadows sufficiently strongly for half-tone reproduction. Foreign body removed by peroral bronchoscopy.

Comment.—In the light of the subsequent history it is easy to trace the matter of the foreign body; but it must be remembered that the symptoms at the time of its aspiration were exceedingly slight and during the symptomless interval were for-

gotten by the patient in the activities of service at the front; a fact paralleled frequently in other cases even in the serene environment of civil life. The patient's personal history, including pneumonia, measles, an operation under ether, influenza, and gassing, certainly furnished enough common etiologic factors to account for the pulmonary abscess without bringing up the rarer question of foreign body. It is to be noted that the pneumonia antedated the foreign body aspiration. True lobar pneumonia rarely, if ever, follows foreign body. It is interesting to note that even a metallic foreign body may not be visible in a good ray plate. The foreign body, though of metal, was very thin and overlay the heart shadow and an area of pathology; moreover, the patient was a very robust man, with an enormous, well-developed, muscular chest. A person of this type is always the most difficult for roentgenologic study, as shown by the fact that after the foreign body was known to be present, it was only with the utmost skill in roentgenography and interpretation that the for eigh body could be demonstrated. The best one of these roentgenograms is used for the illustration (Fig. 145), and it will be seen that the foreign body had to be outlined in order to show in a half-tone because of the overlying dense shadows of the chest wall, the heart, and the pathologic tissue. We have had 6 cases of pencil cap in the lung. Recovery has followed removal in all.

Case II (Fbdy. No. 1095).—This child, aged three years, had been ill for two years of its short life. The illness started suddenly in February, two years ago, while the previously healthy child was sitting on the floor, with an attack of choking, strangling, coughing, and wheezing. This was followed by fever, and the child was supposed to have a bronchitis which improved at the end of two weeks, but wheezing and occasional cough was noted until summer, when the cough altogether disappeared, though wheezing persisted. The following winter the cough returned, became loose and productive, and persisted all winter. The second summer of the illness the child had what was supposed to be a pneumonia followed by abscess and supposed

empyema, for which external operation was advised to drain the lung. For operative localization a ray examination was made in a distant city and a screw was located in the left bronchus (Fig. 146). On admission here Dr. Manges rayed the child and reported as follows: "There is a small screw in the left bronchus, head down, with the point about the bifurcation of the trachea. There is marked cloudiness throughout the right lung, and at the time of the examination apparently very limited function.

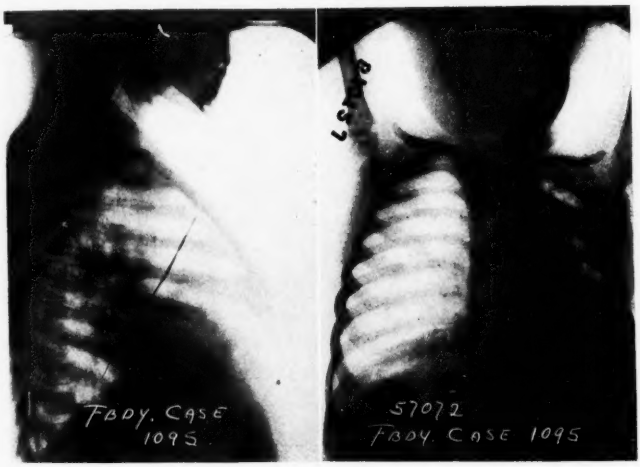

Fig. 146.—Case II (Fbdy. No. 1095). Roentgenograms, anteroposterior and lateral, of a child aged twenty-three months, showing pulmonary abscess caused by the unknown presence of a screw for twenty months. Removed bloodlessly by bronchoscopy through the mouth without anesthesia, general or local, in three minutes and sixteen seconds. (Films by Dr. Willis F. Manges.)

We believe much of this cloudiness is due to retained secretions. There is evidently also considerable fibrosis. I believe that the screw has at times been in the right bronchus. There is at present evidence of a chronic septic pneumonitis in the lower right lobe. The heart is displaced toward the left."

Physical Examination.—The chest is deformed, flattened laterally, with greatest prominence over the lower portion of the sternum. The physical signs elicited by Dr. Edward E.

Graham were as follows: "Left side: Expansion limited and breath sounds diminished over entire left lung, most marked at base; medium sized moist râles everywhere, but most marked in lower two-thirds; resonance impaired especially at base. Right side: Breath sounds unimpaired, numerous moist râles, especially at base. Percussion note unimpaired."

Bronchoscopy.—Without anesthesia, general or local, and with the assistance of Drs. Gabriel Tucker and Louis H. Clerf, a bronchoscopy through the mouth was done a week ago, removing the screw from a bed of bleeding granulations and a pool of pus which welled up copiously as soon as the screw was removed. This pus was aspirated through the mouth with the bronchoscopic aspirator. Time of bronchoscopy, including aspiration of pus and removal of foreign body, was three minutes, twenty-six seconds.

Progress.—A Roentgen-ray examination by Dr. Manges immediately after the removal of the screw and bronchoscopic aspiration of the pus was reported by him as follows:

"Film after operation shows absence of the foreign body. The density in the lower portion of the right lower lobe has cleared materially. There is also air entering the left lower lobe. Heart still remains displaced considerably toward the left."

Today, one week after bronchoscopic removal and aspiration, Dr. Manges reports again as follows:

"The pathology in the left lung has almost entirely cleared up and there is a very marked improvement in the condition of the right side. There is still considerable thickening at the root area on the right side."

Physical examination by Dr. Louis H. Clerf now shows air going to all parts of left lung, including the area that formally was obstructed. On the uninvaded (right) side the râles from the overflow of pus have completely disappeared.

Comment.—The lessons to be learned from this case concern not so much the now accepted facts as to the ease, certainty, and harmlessness of bronchoscopic removal of foreign bodies of long sojourn, but, rather, the invaluable lessons that interest

the general practitioner, the pediatrician, the internist, and the surgeon.

1. As to prognosis, please note the prompt improvement in drainage and aëration of the invaded left lung, as shown by both the physical signs and the Roentgen ray immediately after the removal of the foreign body. Please note also the very great improvement at the end of a week. This is the rule in such cases, and shows that the chief element in the obstruction is the foreign body itself. This is corroborated by the fact that the foreign body at bronchoscopy is found at the *entrance* to the area of lung suppuration. The foreign body is almost never found free in a cavity. Hence its removal from its obstructive position at the threshold of the suppurative area improves drainage so that practically all of these cases get well. Previous experience in many similar cases of lung suppuration following foreign body justifies the opinion that apart from intercurrent disease this child will make an entire and complete recovery; the cough, the deformity of the chest, and the flattening of the fingers will disappear; and within a few years the physical examination and the Roentgen ray will show no abnormality in either lung.

2. *After-treatment.*—The child will be sent home, with advice to the family physician that the child have out-door rest treatment. No local bronchoscopic measures are called for in the after-treatment of lung suppuration when due to foreign body.

3. The choking and strangling and coughing attack noted at the beginning are pathognomonic of foreign body, and even in the absence of any subsequent symptom call for the exclusion of foreign body by physical and radial examination.

4. A previously healthy child suddenly seized with choking, strangling, and coughing *while sitting on the floor* is one of the commonest occurrences in overlooked foreign body cases. The child picks up some object found on the floor.

5. The bronchitis and the asthmatoid wheezing after the choking and strangling complete a picture that is absolutely diagnostic of foreign body in the lung, and call urgently for bronchoscopy even if all the examinations were negative.

6. The rapid clearing of the lung within a week after the

peroral bronchoscopic removal of the foreign body and the peroral bronchoscopic aspiration of the pus, which showed no tendency to reaccumulate, is the rule in such cases, and shows that the foreign body and its granulation bed are the chief obstruction to drainage.

7. The tentative diagnosis of empyema for which thoracotomy was about to be done is one of the commonest occurrences in overlooked foreign body cases, because of the impaired percussion note and diminished breath sounds at the base. Foreign body in the lung should always be very carefully excluded before a diagnosis of empyema is made.

8. Parents should be taught prophylaxis. Children should be trained not to put things in their mouths, and parents should set them a good example, which is better than punishment or precept. Babies should not be put down on the floor to amuse themselves without first seeing that there are no small objects within reach.

Case III (Fbdy. No. 1054).—This patient, a graduate nurse aged twenty-seven years, has had lung suppuration for twenty-one years, accompanied by foul expectoration and hemoptysis, not simply blood-streaked sputum, but hemorrhages such as are seen in cases of pulmonary tuberculosis. No tubercle bacilli have ever been found in her sputum. Since the age of six years the patient had frequent attacks of supposed bronchopneumonia and severe purulent bronchitis. She has suffered continuous ill-health. A metallic pencil cap was discovered and accurately located in a bed of pathologic tissue deep in the parenchyma of the left lung by Dr. Pritchard, of Battle Creek Sanitarium, who referred the case to the Bronchoscopic Clinic (Fig. 147).

Physical Examination by Dr. E. W. Funk.—Definite limitation of expansion over the left lower chest. Percussion note reveals high-pitched resonance on the left side posteriorly from the fifth rib to the base; impaired resonance in left axilla and merging with the cardiac dulness. Over this area at the left base there is diminished vocal fremitus and resonance. Distant breath sounds and occasional fine squeaking râles. Heart is not

enlarged. Action normal. No murmurs. From the physical examination I would venture the opinion that there is a foreign body in the left lower lobe rather deeply situated, perhaps near the heart.

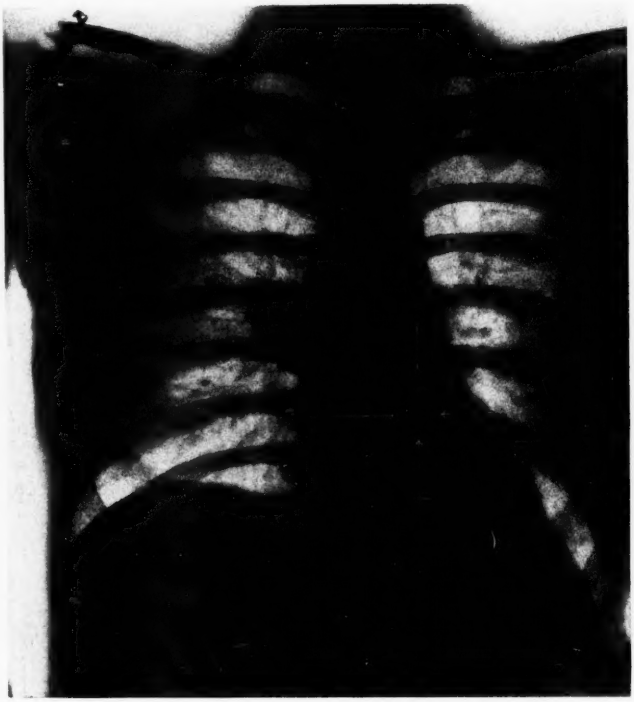

Fig. 147.—Case III (Fbdy. No. 1054). Roentgenogram of woman aged twenty-seven years, showing pulmonary abscess due to a pencil cap that had been in the lung for twenty-one years. Removed by peroral bronchoscopy under local anesthesia.

Bronchoscopy.—Patient being an adult, a little cocain was applied to the larynx. Bronchoscope with accessory drainage canal inserted; copious flow of very foul pus automatically aspirated. Right bronchial orifice noticed to be inflammatory as the bronchoscope passed the bifurcation; left bronchus chronic-

ally inflamed, mucosa thickened. Just below orifice of the left middle lobe bronchus the stem bronchus seemed to be completely obliterated. Forceps were gradually insinuated through organized tissue. Below the narrowing there was a cavity filled with granulation tissue, and it was in this cavity that the foreign body was located, incased in a capsule of fibrous tissue. The foreign body crumbled at the touch of the forceps. Foreign body removed in fragments. During the bronchoscopy the automatic aspirator through its canal in the wall of the tube removed, without a moment's interruption of the work, about 125 c.c. of foul pus. Dr. Manges having located a small fragment of the corroded pencil cap remaining deep down in the lung, we did a second bronchoscopy.

Progress.—Today, four months after the bronchoscopic removal of the pencil cap and the aspiration of the pus from the lung, the patient comes back for re-examination. She reports that the cough and expectoration gradually disappeared. She passed safely through an attack of epidemic influenza which greatly increased the sputum for a time. Dr. Funk has examined her chest and reports, "The signs are normal except for slight limitation of motion over the left lower chest and slight suppression of breath sounds. No râles are audible." Dr. Manges made a Roentgen-ray examination yesterday, and reports as follows: "There is no further evidence of any portion of pencil cap in the lungs, and the inflammatory thickening that was there at the time of removal of the foreign body has now almost entirely disappeared."

Comment.—This case emphasizes the often observed fact of the rapid recovery from pulmonary abscess after the bronchoscopic removal of a foreign body which has caused the abscess, and has, by its bulk, occluded drainage. Such recovery is the rule, not the exception, and is very remarkable in contrast with the tedious convalescence and the often serious prognosis in cases of pulmonary abscess due to causes other than foreign body.

Case IV (Fbdy. No. 1085).—This woman, aged forty-six years, had intermittent productive cough, occasional fever, and

what were thought to be asthmatic attacks since she was eleven years of age. For the past four years the symptoms have been worse. Three weeks ago the patient "felt as though something broke," after which there was a great increase in the quantity of expectoration. The patient was then sent for *ray examination* to Drs. Hickey and Evans, of Detroit, who found a safety-pin in

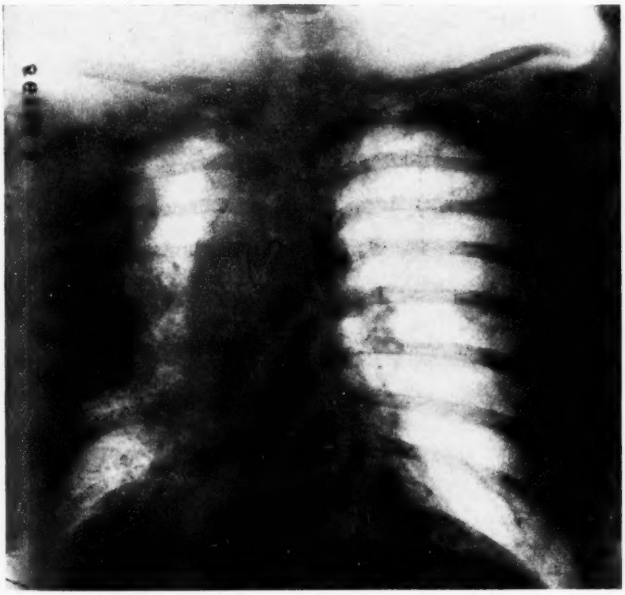

Fig. 148.—Case IV (Fbdy. No. 1085). Roentgenogram showing pulmonary abscess, fibrosis displacement, and extensive pathologic changes due to the overlooked presence of a safety-pin in the lung for thirty-six years. Removed bloodlessly through the mouth, under local anesthesia, in nineteen minutes and seven seconds. (Film by Drs. Hicksy and Evans.)

the right bronchus, with extensive pathologic changes in both lungs and extensive fibrosis, the contraction of which has drawn the heart and mediastinum far over to the right side (Fig. 148). The patient was then referred to the Bronchoscopic Clinic for removal of the safety-pin.

The *physical signs* elicited by Dr. McCrae were as follows:

Expansion limited over entire right chest being practically absent over the lower lobe. Percussion note impaired on the right side over the lower and middle lobes and the lower portion of the upper lobe. Left lung resonant throughout its extent. Auscultation reveals faint, distant, snoring breath sounds on the right side; left side breath sounds harsh, expiration prolonged and roughened, with deep snoring râles both on inspiration and expiration.

Bronchoscopy.—We passed a bronchoscope after anesthetizing the laryngopharynx with cocain and removed the safety-pin in ninteen minutes, seven seconds, most of which time was consumed in searching for a small portion of the pointed branch of the pin in the pus and granulations, in which search we had the invaluable localizing assistance of Dr. Manges. The pin, from its thirty-six years of sojourn in the lung, broke in two pieces when the attempt was made to bring the point into the tube mouth.

Prognosis.—As to prognosis it should be said that the most striking thing in lung suppuration is the phenomenal difference between the prognosis of the lung suppuration due to disease and that due to foreign body. After removal of a foreign body the recovery from a pulmonary abscess is almost invariably prompt as compared to the slow recovery from abscess due to pneumonia or tonsillectomy. Furthermore, the recovery from foreign body abscess is usually complete. Therefore, notwithstanding the extensive pathologic changes in the lung, there need be no hesitation in assuring this patient that she will get well. The after-treatment is by fresh air, rest in bed, preferably outdoors, abundant food of an easily assimilated character—in short, an antituberculous régimen, though this patient has no tuberculosis. The antituberculous régimen is just as effective in any other form of lung suppuration as it is in pulmonary tuberculosis.

Comment.—When told of the pin the patient recalled that when she was eleven years old she had "swallowed" a pin, but it was supposed to have passed with the stools, and the cough not setting in until long after, no connection with the pin was

noted. This case is typical of many others in which a patient has had lung disease for a long time, in this case thirty-six years, without having a Roentgen-ray examination, which would have been advisable, not for foreign body alone, but for the light to be thrown upon any obscure case of intrathoracic disease. This case illustrated clearly that a foreign body should be considered as a diagnostic possibility not only in every case of lung suppu-

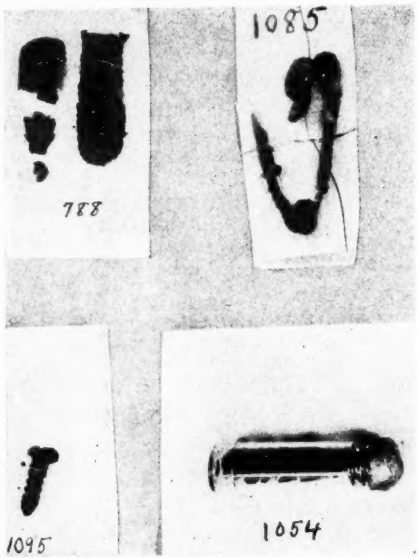

Fig. 149.—Foreign bodies removed bronchoscopically in the foregoing cases. (From the Chevalier Jackson Clinic Collection of 1130 foreign bodies endoscopically removed from the air- and food-passages.)

ration, but in every case of cough, expectoration, and asthmatoid attacks. It also shows the advisability of following up every case of "swallowed" foreign body with a Roentgen-ray examination to be certain that it has not lodged somewhere, and this is necessary even though the foreign body is recovered, because there may have been more than one. The absence of all symptoms, even cough, after a foreign body has been aspirated into

the lung is apt to mislead one to infer that the foreign body could not have entered the lung. This symptomless interval is the rule, not the exception.

Perhaps not 1 per cent. of the patients with an unremoved foreign body in the lung live as long as this woman has. The only reason even she, with an inherited high physical resistance, survived so long was the purely mechanical circumstance that the safety-pin was caught high up in the relatively large bronchus where drainage and aëration of the corresponding lung were not interfered with by the relatively slender pin stretched as a thin wire across the lumen. In later years, however, the secondary pathologic processes impaired drainage and both lungs were being rapidly destroyed.[1] Most cases of metallic foreign bodies in the lung are fatal within a year and a half. A peanut kernel in a baby will be fatal within a few weeks if allowed to remain. A large foreign body in the larynx or trachea may asphyxiate in a few minutes, as hundreds of my clippings from the daily press show.

Conclusion.—In concluding this clinic it may be said that in the Bronchoscopic Clinic we have had 116 traceable cases of lung suppuration due to the sojourn of a foreign body for periods of from one month to thirty-six years, in which the foreign body was removed by peroral bronchoscopy. Of the 116 patients, 110 are alive, and of the 110, all of those brochoscoped prior to one year ago are in good health. These are long sojourn cases. In cases of recently aspirated foreign bodies there have been recoveries in 98.3 per cent. In foreign body work the bronchoscope has achieved results unsurpassed, if equalled, in any other branch of medicine or surgery.

[1] A report received months after removal of the pin states that expectoration has practically ceased, and that the patient has gained 20 pounds in weight.

CLINIC OF DRS. R. M. LUKENS, W. F. MOORE, AND E. H. FUNK

FROM THE BRONCHOSCOPIC CLINIC OF JEFFERSON HOSPITAL

BRONCHOSCOPIC DRAINAGE OF PULMONARY ABSCESSES AND BRONCHIECTASIS

THE object in presenting these 2 cases of pulmonary abscess is to show what can be expected from bronchoscopic treatment of such lesions. These 2 are not ideal cases because of their long duration, and we believe that treatment begun earlier would yield much better results. It is generally accepted that abscesses anywhere in the body which are promptly drained heal more quickly and with a minimum amount of tissue change. Dr. Chevalier Jackson has shown that "peanut pneumonia" is not a true pneumonia, but an "arachidic bronchitis," a suppurative lesion with pus accumulation following the aspiration of a vegetable foreign body, which soon clears up after prompt removal of the cause and establishment of drainage. Abscesses following bronchial obstruction by septic foreign bodies, such as bones and teeth, rapidly clear up after removal of the foreign body. Again, it can be assumed that in pulmonary infections following the aspiration of infected materials, as sometimes occurs after operations on the upper respiratory tract, the early removal of such material should give similar results. The following cases, however, did not follow operation, but measles in early childhood.

While we use the term "pulmonary abscess" in this presentation, we are including bronchiectasis because, while both are definitely distinct and different processes pathologically, from a clinical point of view they represent lung suppuration with localized pus collection, which may be attacked bronchoscopically along the same lines.

CASE HISTORIES

The first patient which we wish to present is a female aged twenty-six years, stenographer, referred by Dr. George Gracey to Dr. Chevalier Jackson May 8, 1922. The chief complaint was cough for the past twenty-three years. The expectoration was thick, yellowish, and foul, and about 8 ounces were raised a day. There have been no fever, chills, night-sweats, hemoptysis, or loss of weight. No history of aspiration of foreign body was obtainable. The patient dates the onset of the trouble to the age of three years, following an attack of measles. The cough was constantly present and always associated with foul, yellowish expectoration. During the past year the cough has become worse, and since Christmas, 1921 hearing has been affected.

She has been under the care of numerous physicians in the past twenty-three years. Medicines have given no relief. The sputum examinations have been repeatedly negative for tubercle bacilli. The *x*-ray examination, about five years ago, by Dr. Richards, of Harrisburg, showed "a cloudy condition of the bronchi not localized."

The physical examination in our clinic showed the following: A well-nourished adult female with no cyanosis or dyspnea. The finger-nails are thick and markedly curved, but no clubbing is evident.

Chest: The expansion is slightly limited on the right side and in the lower half. The other physical signs are shown on the chart. From a consideration of the history, symptoms, and signs, the diagnosis of bronchiectasis involving the right lower lobe was made. The lesion, according to the signs, is probably most marked in the upper half of the right lower lobe. The scattered squeaking sounds in both sides of the chest suggest some generalized bronchitis. The relative clearness of the apices is a point against any active tuberculous lesion.

Nose, throat, and ear examination: The tonsils are moderately enlarged and the pillars inflamed. The left middle turbinate is enlarged and impinges on the septum. No nasal discharge is present, although patient states that her nose becomes filled with foul-smelling pus after almost every coughing attack.

The larynx is negative. Both external auditory canals contain hardened débris. There is pus behind the débris obstructing the left auditory canal.

The sputum examinations have been negative for tubercle bacilli.

The *x*-ray study by Dr. Willis F. Manges on May 8, 1922, revealed a localized dense pathologic process in the lowermost anterior portion of the right middle lobe. Its lower border is sharply defined by interlobar pleura that extends from here toward the hilus. It has the appearance of a chronic lung abscess, with a considerable amount of fibrosis. There is marked thickening at the root of the left lung and heavy peribronchial thickening extending to the left lower lobe, with small area of increased density in the parenchymal portion, perhaps due to organized tissue from old foci of infection. There are numerous calcareous nodules at the roots of both lungs, especially on the right side. There is one very large calcified gland in close relation to the trachea just at the bifurcation. There is no *x*-ray evidence of foreign body or of pulmonary tuberculosis (Fig. 150).

The initial bronchoscopy for diagnosis was done by Dr. Chevalier Jackson on May 11, 1922; his findings are as follows:

Right middle lobe of bronchial orifice normal except for very slight superficial mucosal inflammation; no pus coming up out of the middle lobe. Pus coming from the inferior lobe bronchus. Following the pus stream downward, it was traced to an internal branch of the inferior lobe bronchus. Small amount of pus issuing also from other branch bronchial orifices, but only in very small quantities. Pus continued to come from the internal branch mentioned; its orifice was surrounded with granulation tissue and a swollen flap of mucosa, which at times almost occluded it.

The second case which we wish to present is a male aged twenty-three years, admitted to Dr. Jackson's service at the Jefferson Hospital, June 23, 1922, with a provisional diagnosis of abscess of the lung.

The chief complaint was that of cough, with expectoration of a yellowish sputum, which at times was blood tinged. He has

had profuse pulmonary hemorrhages during the past four years at intervals of a few months.

The *family history* is negative. The past personal history contains the usual diseases of childhood, including measles. He had an attack of influenzal pneumonia in 1918, at which time he was ill one month.

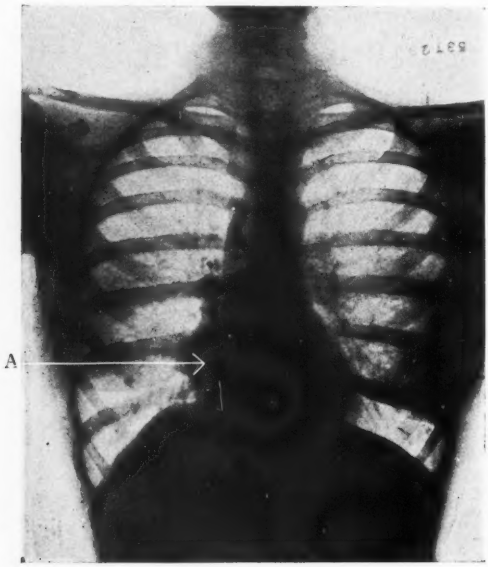

Fig. 150.—x-Ray of chest of Case I shows a chronic lung abscess (A) with a considerable amount of fibrosis in the right lower lobe and the lowermost anterior portion of the middle lobe. Bronchoscopic examination revealed pus coming from the inferior lobe bronchus, but not from the middle lobe bronchus, although there was very slight superficial inflammation around the orifice of this bronchus.

Present Illness.—The patient states that cough with expectoration has been present practically all his life. Since the pneumonia in 1918 he has had pulmonary hemorrhages at about five-month intervals. The sputum examinations have been negative for tubercle bacilli. There is no elevation of temperature

or night-sweats and only a moderate loss of weight. The sputum is blood tinged and odorless.

The notes of the physical examination by Dr. L. H. Clerf, June 22, 1922, are as follows: A poorly developed and nourished adult male. No dyspnea or cyanosis present. There is marked cough with expectoration of purulent material whenever position of patient is changed. The eyes, ears, nose, and throat present nothing of note.

The thorax is narrow and elongated with prominence of right margin of sternum. The anteroposterior diameter is increased. The heart is slightly ptosed, otherwise normal.

Lungs: The expansion is less over entire right chest; the vocal fremitus is equal.

Percussion: There is impairment over the right lung about the nipple, and hyperresonance over the upper right lobe anteriorly. There seems to be an increased resistance over left upper front. Posteriorly there is impairment over the right lower lobe, extending forward to the midaxillary line. The left back is clear.

Auscultation: The breath sounds are clearly heard generally. A few fine crackles are heard in the right axilla and in the right nipple area both on inspiration and expiration. The expiration is unduly prolonged over these areas. The abdomen and extremities with their reflexes are normal. The Wassermann reaction is negative.

The *x*-ray report by Dr. Willis F. Manges on June 24, 1922 showed a sharply circumscribed, apparently inflammatory mass in the right chest at the level of the fifth rib and along the mediastinal aspect of the right lung, probably in the middle lobe, with peribronchial thickening and some bronchiectasis in the right lower lobe along the inner and posterior aspect. There is also heavy peribronchial thickening and slight dilatation of the bronchi in the lower left lobe (Fig. 151).

Bronchoscopy for diagnosis was done by Dr. Chevalier Jackson June 29, 1922. He found pus coming from a posterior branch of the right inferior lobe bronchus. All the bronchi on the left side were inflamed. Swabs were inserted into the

bronchus from which the pus was coming, and two uncontaminated specimens obtained on sponges were sent to the laboratory. The fistulous bronchus had not the appearance of a tuberculous process. The fistula was dilated with expanding forceps.

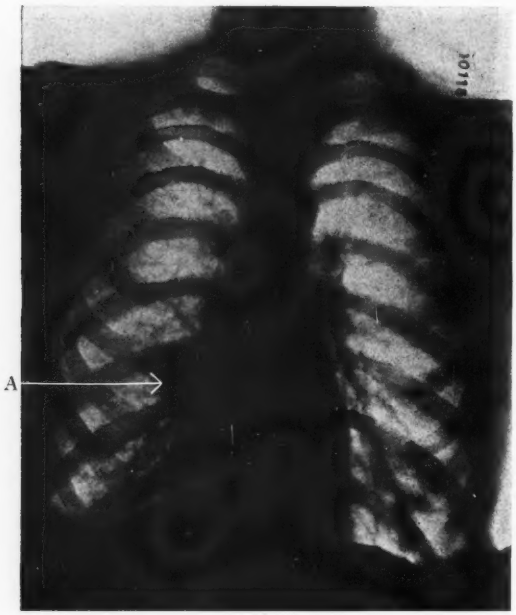

Fig. 151.—*x*-Ray of Case II shows a sharply defined abscess (A) in the right chest at the level of the fifth rib. Peribronchial thickening and some bronchiectasis in the right lower lobe along the inner and posterior aspect. There is also heavy peribronchial thickening and slight dilatation of the bronchi in the left lower lobe.

Diagnosis: Abscess communicating with the posterior branch of the right inferior lobe bronchus.

On July 7, 1922 the patient was referred by Dr. Jackson to the bronchoscopic clinic at the Department for Diseases of the Chest for bronchoscopic drainage and treatment.

The previous patient was referred shortly before, and our studies of the 2 patients cover the same period of time.

In both cases the pus obtained from the bronchi draining the abscess contained streptococcus, staphylococcus, and pneumococcus. Vaccines were made from these specimens and given at three-day intervals, beginning with 750,000,000 of the combined infecting organisms and increasing to 3,000,000,000.

THE TECHNIC OF BRONCHOSCOPIC TREATMENT

Morphin and atropin are given hypodermically one hour before operation; cocain is applied locally in 10 and 20 per cent. solution deep enough in the pharynx to inhibit the superior laryngeal nerve. After the first bronchoscopic treatment morphin and atropin are gradually decreased and finally omitted. At times cocain is applied to the bronchus to inhibit excessive cough.

All secretions are removed as far as possible with the aspirating bronchoscope. The affected bronchus is evacuated with a small calibered suction-tube, which reaches beyond the end of the bronchoscope, and the bronchus is irrigated thoroughly with a solution containing 5 minims of phenol, 1 dram of Lugol's solution in a pint of normal saline solution; latterly we have substituted for the phenol 2 grains of trinitrophenol. This was at the suggestion of Dr. E. Q. Thornton, who in his studies on the action of picric acid was led to believe that this would be more efficient than carbolic acid. In this strength it has proved non-toxic and non-irritating.

A 20 per cent. solution of argyrol was instilled into the affected bronchus on one occasion, but the patient stated that she did not feel as well and coughed more than at the times following the regular treatment. Argyrol was discontinued after a few treatments. For about sixty hours after the argyrol treatments the coughed-up secretions were tinted brown (Figs. 152–154).

In each patient every endeavor was made to secure, in addition to the bronchoscopic drainage, the best possible natural drainage by having the patient sleep on the well side and to as-

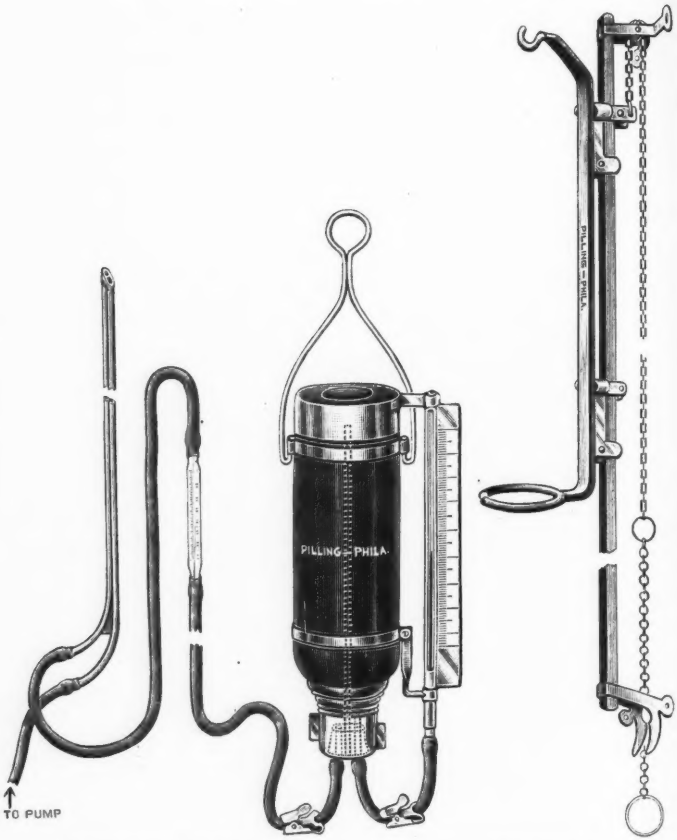

Fig. 152.—Lukens' thermic irrigating apparatus. This apparatus is used in the Jefferson Hospital Bronchoscopic Clinic for washing pus from the bronchi draining pulmonary abscesses and bronchiectatic cavities. It consists of a steel vacuum bottle of 1000 c.c. capacity; to the side is a gage showing the quantity of irrigating fluid contained in the vacuum bottle. A rubber tube leads to the irrigation tube, and has in its course a thermometer so that the operator can see the temperature of the irrigating fluid as it is about to enter the lung.

To the right of the cut is shown the support for the irrigation reservoir, which can be lowered or raised at will to control the force of the irrigating fluid.

(All of the instruments illustrated in this article are made by George P. Pilling & Son Co., Philadelphia.)

Fig. 153.—Bronchoscopic irrigators. These are part of the thermic irrigating apparatus shown in Fig. 152. The uppermost irrigator is a single-way tube and is used when the bronchoscope is less than 7 mm. in diameter; an irrigating bronchoscope must be used with this tube. The two lower irrigators are two-way tubes; one without valves and one with valves for regulating the force of the irrigating fluid and the strength of the suction. The lower, smaller tube is attached to the irrigation reservoir, and the upper, larger tube is attached to the suction-pump. Fluid flows into the bronchus and is almost immediately drawn off together with pus, etc.

sume this position as much as possible during the day. The general hygiene was gone into very carefully. An abundant nutritious diet, as for tuberculous patients, was instituted and an outdoor life prescribed. Both patients gave up confining occupations of their own volition, although we did not insist upon this. The second patient is now back at work.

It is interesting to note that the bacterial findings in the pus changed while under treatment. The second specimen of pus in

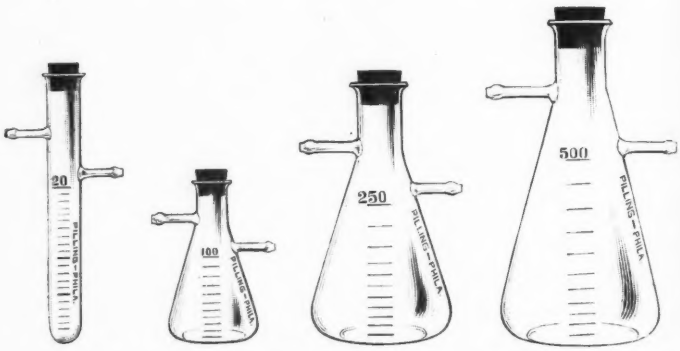

Fig. 154.—Lukens' collecting tubes and flasks. The tubes or flasks are interposed between the suction-tube and the suction-pump and intercept any secretion or pus that may be drawn from the lung or bronchi. The collecting tube is used to collect and measure quantities less than 20 c.c.; for quantities larger than this the flasks are used.

Uncontaminated specimens are obtained in these collectors directly from the affected bronchi and sent to the laboratory for bacteriologic diagnosis and preparation of vaccines.

each instance, obtained two months later, differed from the first in that the pneumococcus and staphylococcus were eliminated, leaving only a pure culture of streptococcus. A pure streptococcus autogenous vaccine is now being given to both patients.

COMMENT

Suppurative disease of the lung frequently results from the aspiration of infected material, hematogenous or lymphogenous infection, or following an acute infectious disease, such as pneu-

monia, measles, etc. Both of these patients seem to belong to the third group. In the first patient the lung symptoms followed measles in childhood, and in the second patient probably measles in childhood aggravated by an attack of influenzal pneumonia in 1918.

In the first patient the frequency of cough has changed from many times during the day, and at night for hours, to from one to three times during the day and none at night, insuring uninterrupted sleep. The quantity of expectoration has diminished from 64 drams in the twenty-four hours to less than ½ dram to 3 drams in the early part of the week to 5 to 6 drams in the last one or two days before the next treatment.

In the second patient the expectoration has likewise been decreased, and the attacks of hemoptysis have become more infrequent and the coughed-up material is no longer blood streaked. The patient has had only one frank hemorrhage since June, 1922, small in quantity, which evidently came from granulations about the mouth of the affected bronchus. The earlier and larger hemorrhages were probably due to erosion of blood-vessels in the abscess wall.

In the first patient the odor of the breath and sputum were so offensive that the patient discontinued all social functions because she felt that it was offensive to others. The odor disappeared after a few treatments and has not returned. She is no longer troubled with expulsion of pus into her nose. The sputum has changed from one that was thick and tenacious to a much more fluid consistency.

The notes of the physical examination of July 7, 1922 reveal the following: Expansion greatly improved over right lower chest, where restriction previously existed. Percussion note distinctly less impaired. Breath sounds are more clearly heard, and the impression given the auscultating ear is that more air is entering and leaving the affected lung. No râles present except an occasional coarse squeak. The finger-nails are showing a new and more normal growth since the beginning of the bronchoscopic treatments. The nail of the ring-finger, for example, shows a distinct ridge between the old curved nail and the newer

less curved nail. The patient states that the nails are growing more quickly, cuticle is appearing, which was never present be-

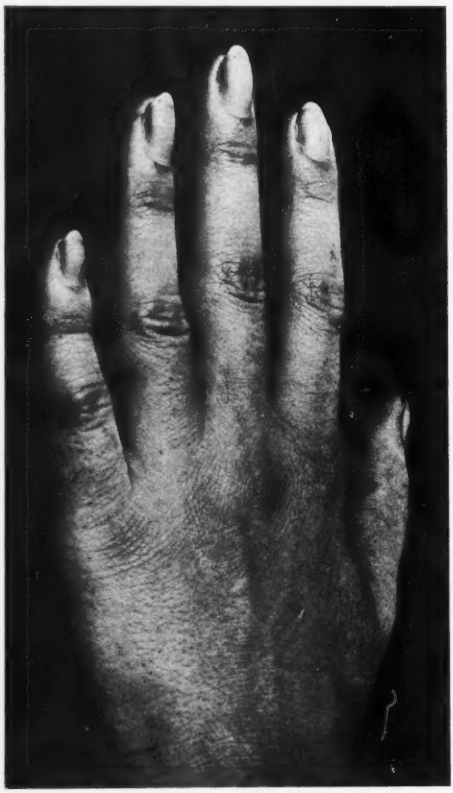

Fig. 155.—Unretouched photograph of left hand of the first case taken July, 1922. The nails are thick, markedly curved, and of a chalky-white color. The lunulæ are just appearing, they were absent when the patient was first seen. The patient stated that they had never been present before. The nail of the ring finger shows a distinct line of demarcation between the old and new nail formation. Indicated by the arrow.

fore, and the crescents are likewise appearing. These were never previously seen. The improvement in the trophic condition of the patient's skin is evidenced by a more normal feel of the

Fig. 157.

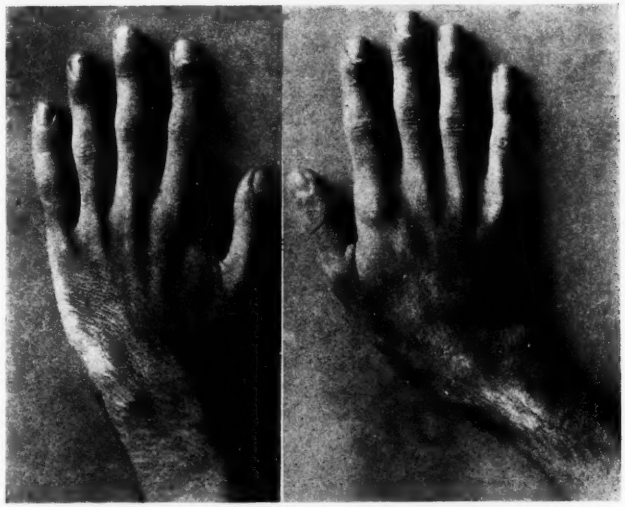

Fig. 158.

Figs. 157, 158 are unretouched photographs of the hands of Case II taken about the same time as those in Figs. 155, 156. They show marked clubbing of the fingers with only slight change after three months of bronchoscopic treatment. Improvement in nutrition is shown by a more plump appearance in Fig. 157.

skin generally, and to an increased growth of the hair on the head, which has been distinctly noticeable to the patient. She

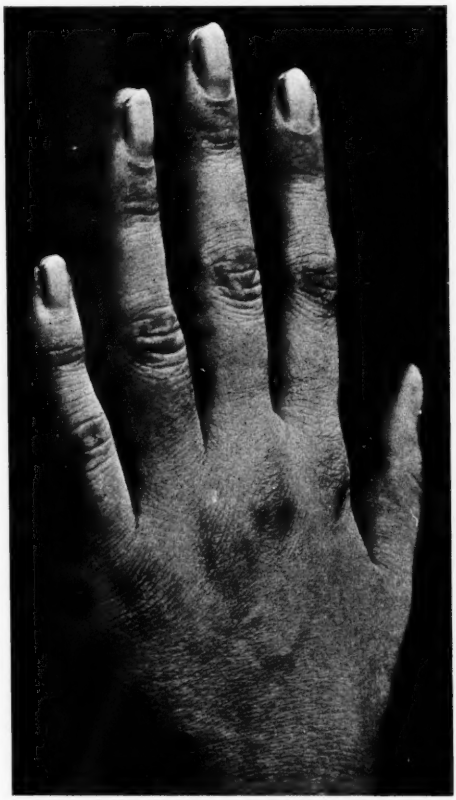

Fig. 156.—The same hand as Fig. 155. Unretouched photograph taken October, 1922. The nails are much more flattened, and thinner; note especially the nails of the index, ring, and little fingers. The color of the nails is almost normal, and the lunulæ are quite prominent in the nails of the index and second fingers.

is very high in her expressions of appreciation of the beneficial effects of the treatment. Four months later—*i. e.*, November 24, 1922—all the signs of improvement continue (Figs. 155–158).

The physical examination of the second patient November 11, 1922 reveals an improvement in the general appearance of the patient, a gain in weight of 5 pounds, no dyspnea, no cyanosis, tongue slightly coated. The chest examination is noted as follows:

The expansion generally is limited, especially on the right side and in the lower portion of the chest. Posteriorly from the fifth dorsal spine to the angle of the scapula on the right side is a definite impairment in the percussion note. The breath sounds over this area are indistinct, with some prolongation of expiration. Over the entire lower right chest posteriorly and in the lower axilla are heard some coarse squeaking râles and a few fine crackles. Over the remainder of the chest are heard occasionally these squeaking râles. Heart examination shows noting of note.

In this patient an *x*-ray examination, November 13th, by Dr. W. F. Manges, demonstrated that the area involved was relatively less dense and the structures could be outlined showing better drainage and aëration.

Neither patient has suffered any ill effects from bronchoscopic treatments. Both were able to leave the hospital in two hours after the treatments.

From the standpoint of the improvement in the general nutrition, the improvement in the cough and reduction in the expectoration, with disappearance of the odor, we feel that these patients have derived a great deal of benefit from bronchoscopic drainage. Medical treatment had been of no avail and the condition was becoming progressively worse before bronchoscopic treatment was tried.

Surgical treatment, with its high mortality and uncertainty as to cure, should be considered only as a last resort.

CLINIC OF DR. ALBERT E. BOTHE

From the William Pepper Laboratory of Clinical Medicine, University of Pennsylvania

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STAPHYLOCOCCUS AUREUS SEPTICEMIA

There have occurred in the University Hospital during the past few years 9 cases of infection by staphylococcus in which a condition of bacteremia has been established by blood-culture. The gravity of septicemias of the kind and this collection of cases naturally stimulated a desire to explain them and to study their treatment more carefully. There also have appeared two methods of therapy which have seemed to be followed by some clinical improvement. Having summarized our experience with these cases and methods, it seemed profitable to put them on record, and in the following pages they will be found analyzed from the standpoint of infection atrium, the symptoms and their history, bacteriology, and treatment.

Our cases comprise the following:

Case I.—M. K. Aged forty-two years. W. F. M. Admitted to the University Hospital 11/25/19, on the service of Dr. Stengel, for weakness, nausea, and vomiting. She had been in good health until three weeks ago, when the present trouble started rather suddenly with nausea and vomiting. These spells were usually brought on by taking food and continued until the patient was unable to retain even water in her stomach. One week after onset her physician diagnosed the condition as being a result of pregnancy, and a curetage of the uterus was performed. The symptoms of nausea, vomiting, and increasing weakness persisted for the following ten days, when the patient was referred to this hospital. Her previous medical history was negative until last year, when she had an instrumental

delivery at term complicated by a unilateral mastitis. A physical examination on admission shows a well-developed adult female appearing to be in fairly good health. There is an inversion of the nipples, especially of the right. The heart is negative except that the second aortic sound is much accentuated. The blood-pressure is 175 systolic and 100 diastolic.

The urinary examinations showed a specific gravity ranging from 1003 to 1012, and a constant cloud of albumin with wide hyaline, light granular, and leukocytic casts, every specimen being loaded with red blood-cells, leukocytes, and many epithelial cells. Two catheterized specimens of urine were cultured, and from them Staphylococcus aureus (hemolytic) was recovered. The phenolphthalein test (intravenous): first hour, 20 per cent.; second hour, 30 per cent.; total, 50 per cent. Blood-counts were made daily and ranged as follows: Red blood-cells 4,230,000 to 3,210,000, white blood-cells 12,200 to 6500, hemoglobin 78 to 64 per cent.; differential, polymorphonuclears 68 per cent., lymphocytes, 24 per cent., large mononuclears 5 per cent., transitionals 3 to 72 per cent. polymorphonuclears, 18 per cent. lymphocytes, 3 per cent. large mononuclears, 4 per cent. transitionals.

A gynecologic examination was made, and she was found to have a dilatation of the external os which received one finger. The cervix was slightly softened. The uterus was retroverted, and there were marked lacerations of the pelvic floor. Considering the fact that she had curetment ten days ago, the gynecologist doubts the possibility of present pregnancy. The cervix, however, appears as one of early pregnancy.

Further developments during her stay in the hospital were severe pain in neck and shoulders and a systolic murmur at apex. Her condition was manifestly that of a severe general infection. She ran a rather stormy course until 1/5/20, which was about one and a half months after admission. Her temperature ranged from 98° to 103° F. During the last two weeks of her stay she felt very much improved, but still showed a slight rise in temperature, going as high as 99.4° F. Her general improvement was quite satisfactory and as she was anxious to return home

was discharged. Two blood-cultures were taken prior to 1/5/20, both being positive for Staphylococcus aureus (hemolytic). This case, manifestly one of a severe general infection with nephritis, did very well notwithstanding her treatment was only palliative.

Case II.—D. H., aged twenty-three years. W. F. M. Admitted to the University Hospital 1/16/22 on the service of Dr. B. C. Hirst for bleeding from vagina and pain in right side. She had been in good health until five days previous, when she slipped and fell down stairs, three hours following which she had severe pains in lower abdomen and region of stomach. The following day she had a miscarriage, after which she felt well and was free from symptoms for two days, except for bleeding. Two days before admission she complained of pain in lower left side of abdomen, following which she was very prostrated and dyspneic. The pain in the left iliac fossa became quite severe, and for the first time she had several attacks of vomiting. A physical examination on admission shows a well-developed female somewhat stuporous and appearing to be very sick. The heart was not enlarged on percussion, the action being rapid, but weak. There were no murmurs heard. There was marked rigidity over the entire lower abdomen. Peristalsis was entirely gone. From the nature of the case and the suspicious circumstances it was thought that the abortion was self-induced. The patient lived but two days after admission to the hospital. During this time the urinary examination showed a specific gravity of 1015, with a trace of albumin and 3 to 5 granular casts per low-power field. In a blood-culture taken on admission a very free growth of the Staphylococcus aureus (hemolytic) was found. Red blood-cells 3,230,000, white blood-cells 36,700, hemoglobin 55 per cent. The temperature was a septic type and ranged between 99.6° and 102.8° F. until just before death, when it rose to 105° F. This case, like Case I, was evidently secondary to an induced abortion. The general infection, however, took a much more severe course. From the time of admission to the time of her death, two days later,

she was profoundly sick, never regaining consciousness. There were no salient features in the treatment, it having been palliative.

Case III.—J. R., aged forty-one years. W. F. M. Admitted to University Hospital 11/23/21 on the service of Dr. B. C. Hirst, complaining of sharp pains in left side of abdomen. About one month previous she had attempted an abortion, with no effect until five days before admission, when she aborted. At the same time she complained of intense headaches and vomiting. On day of admission she was suddenly taken with a severe chill, rise in temperature to 103° F., and appeared to be in a very toxic state. A physical examination on admission showed a well-developed adult female in somewhat stuporous state. The positive physical findings were in the region of the lower abdomen, where there was some rigidity, slight tenderness, and a moderate amount of distention. An old cystocele and a rectocele were present. The uterus was enlarged, but in good position. The clinical diagnosis on admisssion was incomplete abortion (self-induced).

The following morning a small amount of decidua was removed from the uterus, insufficient, however, to account for the patient's condition, which at this time was quite poor, the temperature being 104° F. and the pulse ranging from 120 to 140. The blood was cultured and a pure growth of Staphylococcus aureus (hemolytic) recovered. The patient died the morning following the operation. This profoundly toxic rapid case was similar to Case II. The onset was probably synchronous with the admission, at which time she had a sudden severe chill. The toxemia was so profound that the treatment was only expectant.

Case IV.—I. G. S., aged fourteen years. W. M. S. Admitted to University Hospital 9/18/21, on the service of Drs. Stengel and Pfeiffer, for fever and pain in the right groin. Since the first of June, that is, over three months ago, the patient has had frequent attacks of furunculosis involving arms, legs, neck,

and abdomen. Never has this condition incapacitated him, and, except for the local discomfort, he has felt quite well. On 9/3/21 he was taken rather suddenly with a severe chill, which was followed by fever. He remained in bed, his temperature being 102° F., and he felt quite weak. On 9/13/21 he first complained of slight pain in right inguinal region. This progressively increased in intensity, and at times took on a sharp shooting character. Associated with this, on admission, there was a slight pain on the opposite side of abdomen. His previous medical history is negative except for an attack of pleurisy on right side three years ago. A physical examination on admission shows a well-nourished, fairly well-developed boy, mentally slightly confused, having hallucinations; he appears to be very acutely ill. Heart was negative, except that it was beating quite rapidly and the sounds were somewhat weak. There was some rigidity of both abdominal recti; tenderness in both iliac fossa; peristalsis interpreted as normal. In the region of the right internal ring there was some fulness which was quite tender. Two boils were present on right forearm, and scars of former boils on both forearms. The results of a study of this case are as follows: The blood-count ranged from 4,400,000 to 3,200,000 red cells. The white blood-cells ranged from 14,600 to 20,000. Hemoglobin from 78 to 60 per cent. The urinary examinations showed a range of specific gravity from 1002 to 1012. A trace of albumin was always present and several granular casts per low-power field. Three catheterized specimens of urine were cultured, and a hemolytic Staphylococcus aureus was grown. The feces were cultured, and the same orgainsm as that found in the urine predominated.

The evolutionary symptoms and findings were fairly numerous. The fulness in right inguinal region soon became more pronounced. It was red, hot, and quite tender. On deep pressure there developed a tenderness over the lower end of the right femur with pain and limitation of motion of right hip-joint. A right inguinal incision was made which revealed a large abscess involving the preperitoneal area of the inguinal region and the space of Retzius. Three boils which had developed on the

left arm were opened at the same time. A few days later an abscess involving the region of the external condyle of the left humerus was detected; then one involving the right ankle appeared, following which there was abscess formation of right parotid gland and osteomyelitis of mandible on same side. After operative treatment on the mandible the general condition of patient was very much improved. He became quite rational, temperature never going above 100° F. Five blood-cultures were taken on different days during his stay in the hospital. All those up to the time of development of osteomyelitis of the mandible were positive for the Staphylococcus aureus (hemolytic). After this his general condition was very much improved, and four cultures, taken at three- to five-day intervals, were negative. On 11/17/21 the temperature rose to 102.6° F., and he complained of considerable pain in right hip-joint. Examination showed slight swelling, limitation of motion, and excruciating pain when pressure was made over this area. The hip was *x*-rayed and diagnosed as osteomyelitis of right pelvis. On 11/18/21 a rather extensive operation was performed involving the pubis and acetabulum, which was quite shocking to the patient, his condition being so grave on the following day that it was feared that he might again have a blood-stream infection. A culture, however, was taken and was negative. All evolutionary foci that were opened were studied bacteriologically, and the same organism was recovered as was found in the first blood-cultures. On 11/19/21 he was given a transfusion of 500 c.c. of blood; after which the temperature rose to 103° F. He became very much weaker and died that afternoon.

Although the patient lived for a sufficient time after the operation in the pelvic region to allow but one blood-culture to be taken, with negative results, the observers of the case felt that no blood-stream infection had reappeared.

The salient feature in the treatment of this case was the giving of fresh bovine staphylococcus antiserum intravenously. It was first administered on 9/22/21, when 50 c.c. were given. A violent reaction immediately followed, with severe chill and

rise of temperature to 105° F., which fell to normal the following morning. The next day it resumed its septic type and on 9/24/21 25 c.c. was again given intravenously. This time the reaction was much less severe. On 9/27/21 the medication was again repeated with a dose of 25 c.c. This was followed, as when first administered, with a very severe chill, the temperature rising to 104° F., and the general condition becoming so poor that vigorous stimulation was necessary. From this time until the development of signs of osteomyelitis of the mandible the temperature remained down, and his general condition progressively improved. Four blood-cultures were taken and each remained sterile.

Case V.—M. R., aged ten years. W. M. R. Admitted to the University Hospital 10/8/21 for pain in left knee. The patient first complained on 10/3/21, when he had hyperpyrexia and attacks of vomiting. He was able, however, to hobble about until 10/6/21, when his knee became swollen, red, and tender; fever rose to 104° F., and he was somewhat delirious. He had severe muscle pains in back, shoulders, arms and legs, and severe headaches. Dyspnea was such that propping up in bed was necessary. There is nothing of importance in his past medical history except that he had frequent attacks of tonsillitis. A physical examination on admission showed a well-developed fairly well-nourished boy of ten years, face flushed, and, in general, appeared to be quite sick. The eyelids were partly closed; he was breathing through the mouth and sweating quite freely. The tongue was coated, dry, and inflamed, the tonsils swollen and red. There were many enlarged and tender lymph-nodes in the anterior chain of the neck. The apex-beat of the heart is in the fifth interspace at the nipple line and is quite diffuse. Cardiac dulness extends 1 cm. beyond the nipple, but the sternohepatic angle shows no alteration. The heart-rate was rapid—140—and not very forceful, but the rhythm was good. In the third interspace to the left of the sternum was a very loud friction-rub which was heard over entire precordium. There was also a blowing systolic murmur

at the apex. The abdomen was distended and tympanitic, with some tenderness and rigidity in the right iliac fossa. The left knee was held flexed. It was slightly swollen and very tender to the touch. Patient's general condition rapidly grew worse. Three blood-cultures were taken at two-day intervals, all being positive for Staphylococcus aureus (hemolytic). The evolutionary findings were pericarditis with effusion, which was opened and drained; pneumonia involving left lower lobe; abscess of right shoulder, abscesses over both buttocks, abscess at left elbow, abscess of right parotid gland, abscess of both ankles, and osteomyelitis of the mandible and femur. The bacteriologic findings of all these lesions proved them to be due to the same organism as that found in the blood-stream, the Staphylococcus aureus (hemolytic). The urinary examinations showed a specific gravity ranging from 1005 to 1022, and a trace of albumin was present in all specimens, with an occasional granular and hyaline cast. Two catheterized specimens of urine were cultured, and the same organisms found as that in the blood-stream. The temperature during the patient's stay in the hospital was of a septic type, ranging from 98° to 103° F., except at times following serum treatment, when it reached 105° F. For four days before discharge from hospital, however, the temperature remained at just about the normal line. He came to the dispensary for dressing of wound for several weeks, and was finally discharged cured.

As soon as the first blood-culture was reported positive for staphylococci he was given 50 c.c. of fresh antistaphylococcus bovine serum. A severe chill followed, after which the temperature rose to 105° F. and fell to 99° F. on the following morning, where it remained umtil the report from the second blood-culture was obtained. This being positive for the same organism, a second dose of 50 c.c. of serum was given. This time, as before, he had a severe chill and the temperature rose to 104° F. After this the temperature ranged between 98.8° and 101° F., and the blood-culture again was positive. After an interval of five days he was again given 50 c.c. of serum. This time he had a chill, but it was not nearly so severe, and the tempera-

ture only rose to 103° F. A two-day interval was given, during which time the temperature remained between 98.6° and 101.8° F. A fourth dose was then administered, which was followed by a slight chill and rise in temperature to 102° F. For the next six days the temperature ranged between 98.8° and 102° F. Then it rose to 103° F. A blood-culture was taken, and it was again positive for the staphylococcus. Serum was again given, with no reactive results in so far as chill or rise in temperature was concerned. From this time up to four days before his discharge his temperature ranged between 98.8° and 102° F., with an occasional rise to 103° F. This represents a convalescent period of about three months, during which time five blood-cultures were taken, each one having been negative. Although his general condition, as one might assume, had become quite poor by this time, nevertheless he had sufficient resistance left to withstand the prolonged infection and overcame the anemia and wasting. After four days of normal temperature he was discharged.

Case VI.—M. R., aged fifteen years. W. M. S. Admitted to the University Hospital on the service of Dr. Stengel for pain in the joints and fever. He had been in good health until twelve days ago, when the present trouble started with drowsiness and loss of appetite. The next morning his left elbow became painful and swollen; eight days later the right elbow also became painful and swollen, after which the right shoulder was involved. His previous medical history was negative except for pneumonia about seven years ago. A physical examination on admission showed a somewhat thin boy of fifteen, cheeks flushed, and perspiring freely. The joints involved were red, swollen, tender, and hot. The diagnosis on admission was acute rheumatic fever. A blood-culture was taken three days after admission and reported positive for Staphylococcus aureus. This was repeated two days later, with the same result. The patient was seen by Dr. Piper, who advised the giving of 1 per cent. mercurochrome intravenously. The blood counts varied from 4,540,000 to 3,800,000 red cells, the leukocytes from 14,000 to

11,700, the hemoglobin from 74 to 56 per cent. The average differential counts were 79 per cent. polymorphonuclears, 16 per cent. lymphocytes, 3 per cent. large mononuclears, 1 per cent. transitionals, 1 per cent. eosinophils. The urine examinations showed a range in specific gravity from 1025 to 1017, a cloud of albumin, casts, red blood-cells, and leukocytes always being present.

The treatment in this case was 1 per cent. mercurochrome intravenously, as advised by Dr. Piper. The results were somewhat spectacular, in that after the second medication the temperature remained low. Localization of the organism, however, manifested itself a short time later in the form of osteomyelitis of the ulna. This was treated surgically and the same organism found as that which was in the blood-stream. Although this case is still in the hospital, the clinicians and surgeons feel that since his general condition is so good, and two blood-cultures have been negative, his blood-stream is free from the organisms.

Case VII.—F. M., aged thirty-six years. W. M. M. Admitted to University Hospital on 11/26/19, on the service of Dr. Stengel, for pain in the back. Since about two months before admission the patient has had severe crops of boils most marked on the back of the neck, where there are still some unhealed lesions. On the morning of 11/22/19 the pain in lower right lumbar was first noticed. It was a constant dull ache which became stabbing in character on the slightest movement. Associated with this he was feverish and had some nausea and vomiting. His previous medical history was negative, except for pneumonitis in October, 1918. A physical examination on admission showed an adult white male of about forty years, well nourished and well developed, very feverish, and face flushed. There were scars of two furuncles on the back of the neck, also a few small pustules. There was a systolic murmur heard at the apex, rather soft and blowing. There was also a systolic murmur heard at the base of the heart, more plainly over the pulmonary area. The other observations were negative,

except that to the right of the lumbar spine in the hollow of the back there is an area which is tender on pressure, and a similar spot at the corresponding point on the opposite side. There is a small blistered area over the right buttock just below the tender spot.

The red blood-cells showed little variation in count, averaging 4,400,000. The white blood-cells range between 14,400 and 16,500. The hemoglobin remained at about 90 per cent. There were 92 per cent. polymorphonuclears and 4 per cent. lymphocytes, large mononuclears 1 per cent., transitionals 2 per cent., and eosinophils 2 per cent.

The urine always showed a cloud of albumin, many red blood-cells and leukocytes, but no casts. The specific gravity ranged from 1005 to 1020. Ten days after admission a furuncle developed over inner end of the clavicle. His condition became gradually worse. He was profoundly toxic and delirious. Twelve days after admission râles and friction sounds were heard at right base, with signs of partial consolidation and possible pleural effusion. Fourteen days after admission redness and swelling developed over outer aspect of right elbow; seventeen days after admission a deep-seated abscess over manubrium appeared; eighteen days after admission tenderness began in left knee, left elbow and right shoulder, and for several days a soft swelling grew in the lower lumbar region, which proved to be a deep-seated abscess. Two blood-cultures were taken, and all flasks contained Staphylococcus aureas, with no hemolysis. Two catheterized specimens of urine were cultured, and the same organism as that recovered from the blood-stream was found in pure culture. The treatment of this case, like that of Case I, was of the expectant type. The temperature in this case was a septic type, ranging between 100° and 104° F. until the signs of pneumonia appeared, when it rose to 105° F. and came down gradually, reaching 100° F. on the fifth day, after which it took on a septic nature, and ranged between 98° and 102° F. until 1/13/20, when the patient died.

Case VIII.—C. J. P., aged seventy years. W. M. M. Admitted to the University Hospital 10/14/21 on the services of Drs. Deaver and Wood. He had been in good health until one week ago, when he complained of pain and swelling in the back of the neck. This tenderness progressively increased and was very acute when he was admitted to the hospital. His condition was diagnosed as due to a carbuncle of the neck, for which he was operated upon by Dr. Wood, after which he became progressively better, and was discharged on 10/19/21. The wound appeared quite clean and granulated well at the base. It was dressed daily up to 10/23/21, on that day the dressing having been omitted. The next day the patient had slight chill, his temperature rose to 104° F., and he felt quite sick. He was advised to return to the hospital. Blood-culture was made and over 100 colonies per cubic centimeters of blood of Staphylococcus aureus (hemolytic) developed. He was given 25 c.c. of antistaphylococci bovine serum. His temperature rose to 104° F. and dropped to 100° F. the following morning. Another blood-culture was taken, in which the number of colonies per cubic centimeter were reduced to 25. He lived but three days after admission, during which time his clinical picture was always that of a profound infection. His temperature was always of a septic type ranging between 99° and 102° F. except immediately after the receiving of serum, when it rose to 104° F. A blood-count was made on admission, being 4,700,000 red blood-cells, 12,600 white blood-cells, 80 per cent. hemoglobin, 87 per cent. polymorphonuclears, 10 per cent. lymphocytes, and 3 per cent. large mononuclears. There were no other positive findings and no evolutionary signs, except that his weakness and toxic state rapidly became worse up to the time of his death.

Case IX.—R. T., aged twenty years. W. F. S. Admitted to the University Hospital 7/7/14, on the service of Dr. Deaver, complaining of swelling of left face and high fever. She had been in good health up to a few days ago, when she scratched a pimple on her lip. The region soon became painful, red, and

swollen. The inflammatory process progressed and extended up the face, involving the eye, it being so great that on admission her features were distorted. On admission the temperature was 103° F. There was delirium and at times stupor. Physical examination was negative except for findings at focus of infection. A blood-culture was taken and reported positive for Staphylococcus aureus with hemolysis. The blood-count showed 3,400,000 red blood-cells, 11,000 white blood-cells, and 80 per cent. hemoglobin. The urine showed a cloud of albumin and many casts of all kinds. On 7/8/14 patient became quite restless, then delirious, and died. The temperature never came below 102° F., and just before death rose to 104° F. The treatment was entirely expectant.

DISCUSSION

The foci of infection in these cases divide themselves somewhat as follows: Three of these were secondary to induced abortion (Cases I, II, and III), three were secondary to crops of bolis (Cases IV, VI, and VII), one secondary to tonsillitis (Case V), one secondary to a carbuncle (Case VIII), and one secondary to an infection of the lip and face (Case IX). This gives a rather extensive variation as to foci, but one cannot help but feel from this that wherever staphylococci are present, if conditions are favorable, there may be the portal of entry into the blood-stream, whether it be through the skin or mucous membrane. As to the most favorable forerunner for a staphylococcic infection, trauma presents itself as the most important and favoring factor in the excitation of a staphylococcic septicemia. Our first 3 cases, which followed induced abortions, were, without doubt, secondary to trauma. Quiescent invasions or localized germs may be incited to activity or dissemination by manipulation. The invasion of the organisms into the blood-stream seems, however, to be dependent in part upon the resistance of the leukocytic zone, the permeability of which depends somewhat upon manipulation. Case IX is an excellent example of dissemination after manipulation. This case started with a small pimple on the upper lip, from which,

after picking the surface, an inflammation spread over the face into the blood-stream. Walton Marten,[1] in his recent article on infections of lip and face, brings out beautifully how deadly the apparently insignificant act of picking or squeezing a pimple on the lip may be. He refers to pimples of lip and face as being very common starting places for staphylococcemias, not that the organisms are more virulent in that region of the body, or that pimples are much more common, but because an eruption on the lip or face is obnoxious, so that an attempt is made to clear it up as soon as possible by picking or squeezing, a procedure that may disseminate bacteria in the very vascular facial subcutis. In Case VIII we assume that at the time of excision of the carbuncle organisms gained entrance to the surrounding tissues. When the wound was not dressed the additional pressure from damming back of the pus was enough to bring about a dissemination of the organisms into the blood-stream. The cases with crops of boils as forerunners to the septicemia give no history of exceptional manipulation. At the same time it seems that at the time of the incision for drainage any exceptional pressure which might cause a break in the leukocytic zone may well have been sufficient for dissemination of the organisms. Giami's[2] work on the formation and resistance of the leukocytic zone experimentally is of interest in connection with these cases. He soaked filter-paper in a virulent culture of anthrax bacilli; then laid a piece of filter-paper as gently as he could on the surface of fresh wounds two, six, eight, ten, and fourteen hours after the division of the tissue. If by the slightest roughness the protecting wall of leukocytes, which had already formed at the end of two hours, was broken, this being recognized by slight signs of hemorrhage on the paper, the animal died. Even at two hours a third of the animals survived; at the end of fourteen hours the wall was strong enough to resist these gentle manipulations and all recovered. We know that about every focus of infection a wall of leukocytes is rapidly formed. On the integrity of this wall depends whether or not the micro-organisms advance into the tissues. This wall is at first very delicate, but as time passes it becomes better and better es-

tablished. Rosenbach[3] suggests that the anatomic relation of the muscles of the skin and the cellular tissue is such that infectious material is forced and pumped into the neighboring connective-tissue framework. So it seems that infections, when localized ever so insignificantly as they may seem, should have as little manipulation as possible.

SYMPTOMATOLOGY

The symptomatology of a staphylococcic infection is so far from uniformity that it is not profitable to attempt its description with the hope of being diagnostically positive. Nevertheless it seems that the onset is usually very rapid, being ushered in by a chill, malaise, fever (103° to 104° F.), and great prostration. The picture at any time may be very fulminating, and the toxemia so great as to make it impossible to get a history directly from the patient. There are, however, three factors which were always present in these cases: (1) fever, (2) leukocytosis, which was not over 14,000 in 4 cases, (3) a positive blood-culture. As to variable symptoms, they may be nausea, vomiting, pain in back and head, large spleen, lassitude, and delirium, etc. On studying this collection of symptoms, it boils itself down to but one finding, which is really indicative of staphylococcemia, and that is the finding of organisms by culture of the blood-stream. The above-named features, however, gain greater weight if they succeed upon an infection already known to be due to the staphylococcus.

The urine examination of all these cases on admission gave evidence of nephritis. Albumin, casts of all types, red blood-cells, leukocytes, and specific gravities ranging from 1002 to 1024 were constant findings. From this one seems almost justified in including nephritis as a constant associated finding, but since we had no evidence as to the condition of the kidneys before the admission of these patients to the hospital, it is difficult to estimate the rôle of the staphylococcus in the production of a true nephritis. The fact that in all the cases from whom we obtained catheterized specimens of urine the same organism as that found in the blood-stream was grown makes it entirely

credible that definite pathology exists, especially when taken in combination with the urinary findings. Just what these pathologic changes were is hard to say, since autopsies were not made on any of these cases. Nevertheless, I feel that we might be justified from our findings in considering the pathology to be a degenerative tubular nephritis as described by Stengel and Fox.[4]

EVOLUTIONARY SYMPTOMATOLOGY

If one thinks of the possibilities of evolutionary symptoms in cases of staphylococcemia it becomes almost an endless chain of involvement. The interesting feature, however, in these cases is the way they attempt to divide themselves according to the age of the subject. In the adolescent a generalized staphylococcus infection means osteomyelitis, but in the adult a staphylococcemia is diagnosed with difficulty, owing to the variability of the localizations of the infectious agents, the evolution of the process assuming the superacute, acute, subacute, or chronic form. In all of our adult cases the diagnosis was always obscure and was made certain only upon finding the organisms in the blood-stream. The onset was so much like that of pneumonia, or typhoid fever, or any other generalized infection that never could one venture a positive diagnosis until the blood-culture had been found positive. In the adolescent, however, the picture was somewhat different. In these cases, a generalized staphylococcic infection almost always means osteomyelitis; and, vice versa, an osteomyelitis must mean a former blood-stream infection. In the 3 cases in this series it was one of the outstanding features that developed. It is so constant an evolutionary finding that one might justly assume that all cases of osteomyelitis are a result of blood-stream infection and usually the staphylococcus. I say "staphylococcus" because in all of the cases in this series which developed osteomyelitis the locally responsible organism was the same as that found in the blood-stream, and they all developed after a positive blood-culture was obtained.

The cardiac findings in Cases I, V, VIII, while not definite, seem worthy of some attention in so far as the possibility of a

staphylococcus endocarditis having developed from the blood-stream infection is concerned. All 3 of these cases had systolic murmurs which were heard best at the apex and developed after the diagnosis of staphylococcus had been established. Lamb and von Glahn,[5] in a report of 3 cases of staphylococcic endocarditis, state that their cases showed no evidence of an old endocarditis before having had a staphylococcemia, and that this holds true for most of these. They claim that the most important aid in diagnosis of an endocarditis, once a staphylococcemia is established, is the development of a new cardiac murmur or some alteration in the quality of an existing murmur. In our cases the murmur was a new development, but underwent very little alteration during the course of the septicemia, and since no further studies were possible in so far as postmortem examination is concerned, it remains somewhat indefinite. Nevertheless since Case V developed such an extensive pericarditis so extensive that drainage was made, I feel we are justified in assuming that an endocarditis most probably existed.

BACTERIOLOGIC STUDIES

The bacteriologic studies were confined to the blood, urine, feces, and foci of infection. The same type of organsim was found in the blood of all cases; the urine was cultured in 4 and the same organism found. The feces were cultured in but 1 case. In this the predominating organsim was identical with the one found in the blood-stream. All foci of infection were cultured, and they likewise were found to be harboring the same organism as that found in the blood-stream. A study of all these organisms gave rise to the following findings:

1. They were all small Gram-positive cocci.

2. They occurred in pairs, irregular masses, and groups of threes.

3. The colonies on agar slants were opaque, orange, or yellowish white.

4. On blood-agar plates the colonies were round, opaque, orange, smooth, and more distinctly orange in color. In 7 cases there was a definite halo of hemolysis around each colony.

5. In boullion there was a good clouding. The growth adhered to the sides of the tubes, a ring being found at the top, and there was a sediment.

6. The gelatin liquefied after one to two weeks.

7. Acid formed in glucose, saccharose, and maltose, but no gas formed.

These findings we felt justified our considering the organism a staphylococcus with pigmentation. The halo of hemolysis found associated with these colonies when grown on blood-agar led to an investigation as to its cause and possible significance. Orcutt and Howe,[6] in working with horse-blood media and extracts of bacterial enzymes, found that the hemolysis frequently associated with the growth of staphylococci is dependent on the fat content of the media. Their experiments were very convincing and prompted us to try the effect of fat content of media on the hemolysis produced by these organisms.

We obtained some sterile blood from a diabetic whose fat content was 18 per cent. per total volume of blood. Orcutt and Howe's work was done with media made with horse blood and the addition of different kinds of fats, the amount depending upon the percentage desired. The added point of interest in our experiments was that our fat media was made from human blood with a physiologically high fat content.

The media used in this work was made as follows:

1. Blood-agar was made from this specimen of blood obtained from the diabetic with a high fat content and poured into Petri dishes, the proportion being 1 c.c. of blood in 10 c.c. of nutrient agar.

2. The washed red blood-cells of the high fat content blood were added to the serum of a normal fat content blood. Petri dishes were then filled with the same proportions of blood and agar as in No. 1.

3. The serum of the diabetic's blood was added to the red blood-cells of the normal blood, and Petri dishes were filled with same proportions as in No. 1.

4. Blood-agar plates made from the whole blood of the apparently normal patient's blood.

Twenty-four-hour boullion cultures of these organisms were grown on the above-described medias, with the following results:

No. media.	1	2	3	4
5254	+++	++	+++	+
5421	+++	+	++	+
5432	+++	+	++	+
5607	+++	+	++	+
5803	+++	+	++	++
5857	+++	++	++	+
5976	+	+	++	+
5997	+++	+	++	+
6046	000	000	000	000
7071	+++	+	++	+
7062	+++	+	++	+
7260	000	000	000	000

The organisms for this work were those obtained from the blood-cultures and foci of infection. Numbers 6046 and 7260 were non-hemolytic types which were used as controls. The plus signs indicate the degree of hemolysis. From this table one can see that without doubt the influencing factor in the hemolysis is the fat content of the media. What significance this finding may have clinically is rather difficult to say. When we examine the gradual decrease in red blood-cell count in Cases I, II, IV, V and a corresponding decrease in hemoglobin percentage we are tempted to feel that this hemolytic property has some influence in the destruction of red blood-cells.

The next point of interest which these experiments bring up is what influence the fat content of the blood at the time of the septicemia may have in the more rapid destruction of the red blood-cells by these orgainsms. This also is rather difficult to answer definitely, but one might be justified in assuming that a high fat content of the blood would tend to expedite the destruction of the red blood-cells. Another question which arises in connection with this is just what influence the fat has in the presence of extreme vascularity on the virulence of the organism. The frequency of osteomyelitis after blood-stream

infection would almost lead one to feel that extreme vascularity plus high fat content of the bone-marrow has a great attraction for these organisms.

Another rather interesting finding in connection with the bacteriologic studies of these organisms is that of pigmentation. We find that the intensity of the pigmentation is inversely proportional to the number of times they are transplanted directly as to the age of the strain. The following table shows our findings in this work of pigmentation after each transfer:

Case.	1	2	3	4
9/20/21	++++++			
10/20/21	++++++	++++++		
11/15/21	+++++	++++++	++++++	
11/30/21	+++++	++++++	++++++	
12/20/21	++++	+++++	+++++	
1/ 5/22	++++	+++++	+++++	
1/28/22	++++	++++	++++	++++++
2/12/22	+++	++++	++++	++++++
3/ 2/22	+++	++++	++++	+++++
3/27/22	+++	++++	++++	+++++
4/20/22	+++	+++	+++	+++++
5/26/22	++	++	+++	++++
6/15/22	+	++	+++	++++

The plus signs indicate degree of pigmentation, the most intense being 6 plus. These cultures were transferred on to nutrient agar at times shown by the dates in the table, each transfer lowering the intensity of the pigmentation until they almost, but not entirely, approach the albus form. Similar work was done by Walker and Atkinson[7] in Boston, 1916 and 1917. In their experiments, however, they finally obtained a true albus form. We were unable to reach this point with our cultures.

TREATMENT

Although the treatment of staphylococcemias is still a point for considerable discussion, the results with the use of two types of therapy on a few of these cases were somewhat encouraging.

Cases IV, V, and VII, all of which were very virulent, were treated with antistaphylococcic serum intravenously. The first of these (IV), an extensive general infection, was given the first treatment after the blood-culture was reported positive for Staphylococcus aureus (hemolytic). The serum was obtained fresh and three doses of 25 c.c. each were given intravenously at two-day intervals. Within an hour after each injection there was a severe chill, a rise in temperature to 105° F., and a fall to 99° F. about twelve hours later. The temperature again rose on the following day to 102° F. After the third injection, however, the temperature fell to 99.4° F. and ranged between here and 100° F. for about two weeks. The general condition gradually became very much improved, and the mental state quite rational and bright after the last injection. After being free from all symptoms of blood-stream infection for about ten days, he then complained of pains in region of the pubis, which gradually grew worse. An *x*-ray plate was made of this area, and a diagnosis of osteomyelitis was made, after which the condition was treated surgically. The involvement of tissue was quite extensive and the shock at time of operation was quite severe, so much so that he died two days later. Since this patient lived for sufficient time after the operation in the pelvic region to allow one blood-culture to be taken with negative results, and since up to the time of operation he never gave any signs of a recurrent blood-stream infection, the observers of the case felt that death was due to surgical shock. Case V, like Case IV, ran a very similar course, and, like that, was treated with antistaphylococcic bovine serum. The reaction which followed was also similar to the other case, in that the temperature rose and then fell to normal, taking on its septic character about two days after each injection. The first dose, which was 25 c.c. of serum in this case, was raised on the second treatment to 50 c.c. This amount was given five times at two-day intervals. After the last injection the temperature ranged between 98° and 100° F. and the general condition of the patient was somewhat improved. Furthermore, five blood-cultures were taken over a period of three months since the last

treatment with serum, and they were all found to be negative. While the general condition of this patient up to within a week of his discharge was always critical, this condition was believed to be due to obsorbtion from his many foci of localized infection, and no longer from blood-stream infection. No evidence of organisms in the blood-stream was present after the last treatment with serum, and after four days of normal temperature he was discharged cured.

The agglutinative power of the antistaphylococci bovine serum for the staphylococci which were obtained from blood-culture in Case V was compared with the agglutinative power of the blood-serum in Case V and that of the blood-serum from an apparently normal human being.

The results were as follows:

Dilutions.	1	2	3	
1 : 10	+	+	+0	1 equals patient's (Case V).
1 : 20	+	+	+0	
1 : 30	+	+0	+0	2 equals bovine serum.
1 : 40	+	+0	−	
1 : 50	+	−	−	3 equals control normal patients.
1 : 60	−	−	−	

In Case VIII the septicemia, apparently being secondary to the excision of the carbuncle, was of a very severe type. The blood-culture taken on admission had over 100 colonies per cubic centimeter of blood. Twenty-four hours after admission the patient was given 25 c.c. of antistaphylococcic bovine serum. This injection, like those in the two preceding cases, was followed by a very severe reaction and fall in temperature for twenty-four hours. The following day another blood-culture was taken, and the number of organisms per cubic centimeter were found to be reduced to 25. From the time of onset in this case the prognosis was very poor. It was one of those fulminating virulent types which no form of treatment could possibly have saved. The general condition slowly got worse and he died on the third day. While this case never showed

signs of improvement, in so far as his general condition was concerned, from the time of admission, we were of the opinion that the reduction in the number of organisms in the blood-stream after giving the serum was influenced in some way by this treatment.

The other form of treatment which was used in Case VI was the use of a 1 per cent. solution of mercurochrome intravenously. The technic, which is as follows, was first described by Dr. Piper[8] and is a direct copy from his report: "A solution of mercurochrome is prepared with sterile distilled water in 30 to 50 c.c. ampules of 1 per cent. strength. It has been shown by other investigators, which our experience corroborates, that the drug loses its strength unless freshly prepared, and for that reason we have it put up in ampules after we have determined upon its use. We never carry any solution on hand. It should never be used unless the solution is absolutely clear. The adminsitration is done with a fine needle and a large syringe at a temperature as near 100° F. as possible, and the injection made very slowly. Formerly at the end of twelve hours the patient received a dose of magnesium sulphate, but we no longer do this. The reactions are treated symptomatically. We use external applications of heat for the chill and a bismuth mixture as an intestinal sedative for the diarrhea, if it continues too long. A careful record of urinary output must be kept, as it will run below normal owing to the fluid output by the bowel. Subsequent administration of the drug may be made. We make it a rule, however, never to repeat as long as there is any sign of the dye in the urine or bowel movements. We have given as many as five doses."

The treatment of this case was done with a solution prepared as described above by Dr. Piper; two injections being given. The results after this treatment were very encouraging, the blood-stream being free from organisms after the second injection, and the general condition of the patient very much improved.

This is the first case, in so far as I know, of staphylococcemia that has been treated with intravenous mercurochrome. The

cases which Dr. Piper first worked with were of the streptococci forms of septicemia. His results in those cases, like in this one, are very encouraging.

CONCLUSIONS

1. Manipulation is a big factor in expediting the dissemination of localized organisms into the blood-stream.

2. A positive blood-culture is the only sure indication of a staphylococcemia. The commonly associated ones are fever, leukocytosis, and nephritis.

3. The development of the process from its primary focus to its completion passes through stages of multiple abscess formation, osteomyelitis, and endocarditis.

4. The hemolytic power of staphylococci is in some way associated with breaking down of fat, and varies in degree directly as the variability of fat. Pathogenic staphylococcus aureus is usually hemolytic. Recently isolated strains of staphylococcus aureus are deeply pigmented, a character they lose as they grow older under laboratory conditions.

5. Two variteies of specific treatment were used in the cases above reported—antiserum and mercurochrome—both of which seem to have a slightly favorable effect. This was indicated in two ways—an improvement in the clinical condition and a reduction in the number of organisms circulating in the blood.

BIBLIOGRAPHY

1. Walton Marton: Annals of Surgery, vol. i, xxvi, July, 1922, p. 13.
2. Giami: Centralblatt f. Bacteriol., vol. xi.
3. Rosenbach: Archiv. f. klin. Chir., 1905, vol. i, xxvii, p. 715.
4. Stengel and Fox: Text-book of Path., 7th ed., p. 762.
5. Lamb and Von Glahn: Med. Clinics of North Amer., January, 1922, New York.
6. Orcutt and Howe: Jour. Exper. Med., April, 1922, pp. 409–420.
7. Walker and Atkins: Jour. of Med. Research, 1916, 1917, 35.
8. Piper: Amer. Jour. Obst. and Gyn., November, 1922, p. 532.

CLINIC OF DR. RICHARD A. KERN

UNIVERSITY HOSPITAL[1]

INFLUENCE OF INFECTION ON CARBOHYDRATE TOLERANCE IN DIABETES MELLITUS

I. A Case of Diabetic Gangrene.

II. A Fatal Case of Tonsillitis in a Diabetic on High Fat Diet.

DIABETES in persons past middle life is at times considered a rather mild disease. These patients, with little or no diet restriction, enjoy fairly good health for years, often showing only a variable glycosuria, and no tendency to acidosis. Not uncommonly the glycosuria gradually lessens and may finally cease because of progressive renal sclerosis and the consequently elevated threshold for glucose excretion, so that the patient (and at times his physician) is lulled into a sense of false security. But the good health of these cases is more apparent than real. A hyperglycemia of some years' duration has in some manner gradually produced an arteriosclerosis that may be of the most advanced degree. Slowly but surely the blood-supply of an extremity is diminished. A trivial injury gives entrance to a local infection that the undernourished tissues are unable to throw off. Neglect on the part of the patient, and then, only too often, inadequate treatment on the part of the physician permit the development of local gangrene. At once the whole aspect of the case is changed; an apparently mild disease looms up as an imminent threat to limb and life. There is progressive death of tissue and spreading local infection. Absorption of

[1] From the Medical Division of the Hospital of the University of Pennsylvania.

toxic material from the affected limb profoundly influences the patient's general condition; his power to burn carbohydrate rapidly fails, resulting in incomplete fat combustion and consequent acidosis. These factors, in turn, lessen the body's resistance to infection. Even at this stage the process is often not halted, usually because of the patient's refusal to consent to amputation, but at times because of hesitant and inadequate surgery, and the patient finally succumbs to a precipitate coma or a belated high amputation after a sudden flare-up of local infection.

CASE I

The following case well illustrates the effect of the local infectious process on the carbohydrate tolerance: Mr. S. M. H., aged sixty-five, was admitted to the hospital on April 11, 1921. Twelve years before, because of weakness, abdominal pain, and loss of weight and strength, he had consulted a physician, who found sugar in the urine and put him on a diet. Failing to improve, the patient was treated by several other physicians, and finally by an "herb doctor," who for three weeks put him on a strict diet that rendered the urine sugar free. Being thus "cured," the patient remained in good health for over ten years, during which time he was "fairly careful" of his diet. During the early winter of 1920–21 he noticed an increasing thirst. His weight, which in the course of the years had fallen from 240 to 220, dropped another 20 pounds. On December 20, 1920 the patient fell and was badly shaken up. That night he took a hot drink, went to bed early, and put a hot brick at his feet. Next morning the plantar surface of the right great toe, the two adjacent toes, and the left great toe were blistered. A physician evacuated the fluid through a needle puncture and the patient continued at his business. Two days later the toes became painful and at the end of a week began to turn black at the tips. The patient was put to bed and active local measures begun. For a month there was little change. Then his diet was for the first time restricted both as to carbohydrates and fats, and in the course of another month the left great toe healed. During this period the patient's strength was greatly reduced and he

lost a considerable amount of weight. On the right, however, the gangrene slowly spread, extending above the base of the affected toes, and because of this he was sent to the hospital. The previous medical and family history were negative.

On admission the emaciated patient appeared older than his years. The superficial vessels showed an extreme degree of sclerotic change; the radial arteries were hard, beaded, and almost incompressible, and the pulse-wave could scarcely be felt. Blood-pressure readings under these circumstances were open to question. The figures obtained were, however, constantly low—105 to 110 systolic, 65 to 80 diastolic. No arterial pulsation could be felt in either foot. On the right the first three toes and the adjacent part of the foot were involved in a dry gangrene that extended nearly to the instep. In both legs pain sensation was greatly reduced and the reflexes diminished. There were beginning cataractous changes in both eyes. The cardiac dulness was slightly enlarged, measuring 14 cm. across, but the heart sounds, rate, and rhythm were normal. There was no fever. The blood-count was: red cells, 4,610,000; hemoglobin, 80 per cent., leukocytes, 9200, with a normal differential. The blood Wassermann was negative.

Local measures under the guidance of a surgical consultant and diet control were promptly begun.

Table I (p. 1056) presents some of the figures obtained during the first ten days of treatment.

On admission the patient was put on a low-fat, high-carbohydrate diet because acidosis was suspected. Two days later, because of the reassuring CO_2 and ketone figures, the fats were increased to bring up the caloric value of the diet, and the carbohydrates reduced to render the urine sugar free, preparatory to amputation. This was followed by a prompt increase in the ketonuria and the fats were correspondingly reduced. In the meantime the gangrenous lesion was not doing well. The necrosis was steadily spreading, and there was suppuration in the living tissue above, undermining the skin. It was, therefore, decided to attack the glycosuria by starvation. Table II (p. 1056) gives the figures during this period.

TABLE I

Date.	Diet in grams.				Urine.					Blood.	
	Protein.	Fat.	Carbohydrate.	Calories.	Sugar, grams.	Acetone.	Diacetic acid.	Total N.	Ketones, grams.	Sugar, per cent.	CO_2, vol. per cent.
4/12	53	19	95	763	78	mod.+	wk.+	4.25	.71	.230	58
4/14	76	56	17	876	39	mod.+	mod.+	.....	.....	.231	56
4/17	80	26	20	634	21	str.+	mod.+				
4/20	70	23	18	559	25	str.+	str.+	16.6	11.03	.....	45
4/21	69	22	19	550	trace	str.+	str.+				

TABLE II

Date.	Diet: 1200 c.c. clear broth.				Urine.					Blood.	
	Protein, grams.	Fat.	Carbohydrate.	Calories.	Sugar, grams.	Acetone.	Diacetic acid.	Total N.	Ketones, grams.	Sugar, per cent.	CO_2, vol. per cent.
4/22	28	.....	.....	112	trace	str.+	str.+	.....	.....	.....	55
4/24	28	.....	.....	112	str. tr.	str.+	str.+	.....	.....	.200	55
4/25	28	.....	.....	112	5.6	str.+	str.+	9.52	5.7		
4/27	28	.....	.....	112	str. tr.	mod.+	str.+	.....	.....	.172	48
4/28	28	.....	.....	112	trace	mod.+	str.+				

After seven days of fasting the patient still had sugar in the urine, qualitative reactions for ketones in the urine were strongly positive, and the plasma CO_2 had fallen to 48 volumes per cent. Continued advance of the gangrene, slight fever, and the patient's general condition made further delay hazardous. He was, therefore, given a diet with some carbohydrates and little fat; on May 2d the urine still showed strongly positive acetone and diacetic reactions and some sugar, but the plasma CO_2 had risen to 58 volumes per cent. On the following day the leg was amputated a handbreadth below the tubercle of the tibia under nitrous-oxid-oxygen anesthesia. The patient stood the operation very well and his surgical convalescence was quite uneventful.

Table III (p. 1058) gives some figures on the postoperative period.

After the operation a diet low in fat and high in carbohydrate was ordered. The low carbohydrate diet of May 4th was given by mistake, an error that might have proved disastrous. And now developed the most interesting feature of the case. Prior to operation the patient's carbohydrate tolerance was so low that on starvation he was unable to completely burn the carbohydrate fraction resulting from the breakdown of his own body protein and the small amount of protein in the broth. With the removal of the infected focus the power to utilize carbohydrate promptly increased, and this with no particular dietary attempt to render the urine sugar free; in fact, the carbohydrate intake was raised 20 grams. Nevertheless, the glycosuria became steadily less and finally disappeared, as did the ketonuria, and the urine remained normal to the time the patient left the hospital. The day before his discharge he was utilizing a diet with 1544 calories. It had been impossible to weigh the patient prior to operation, but on June 3d he weighed 114 pounds, and by June 17th had gained $4\frac{1}{2}$ pounds.

Before passing on to the next case I wish to interject a few remarks on the etiology and treatment of diabetic gangrene.

The immediate factor in the production of the gangrene is an arteriosclerosis of the usual senile type, but as to the cause of

TABLE III

Date.	Diet in grams.				Urine.					Blood.	
	Protein.	Fat.	Carbohydrate.	Calories.	Sugar, grams.	Acetone.	Diacetic acid.	Total N.	Ketones, grams.	Sugar, per cent.	CO_2, vol. per cent.
5/4	50	12	8	340	6.9	str.+	str.+	3.15	8.27		
5/7	56	15	51	563	trace	str.+	str.+				
5/9	57	16	51	576	10.8	wk.+	mod.+				
5/13	59	16	53	592	5.5	ft. tr.	wk.+				
5/15	67	17	69	697	trace	trace	wk.+	.....	.....	.147	
5/16	67	17	69	697	0	trace	0				
5/18	66	17	69	697	0	trace	0	.....	.....	.150	61
5/22	66	27	69	787	0	0	0				
5/30	92	80	75	1388	0	0	0	.....	.....	.152	57
6/14	92	82	50	1206	0	0	0				
6/16	101	100	60	1544	0	0	0				

the arterial disease we are still quite ignorant. The question arises, Is there any etiologic relation between the diabetes and the arteriosclerosis? It has been pointed out by Joslin[1] and others that the fact that arterial disease is rarely seen in young or middle-aged diabetics is a strong argument against diabetes being a direct causative factor of arteriosclerosis. Furthermore, from a study of the blood-pressure in his series of cases Joslin favors the view that the presence of sugar and acid in the urine does not injure the arteries or kidneys. There are, however, certain facts that point strongly to a casual influence by the diabetes of vascular disease. In the first place, arteriosclerosis is certainly more frequent and usually of a severer degree in diabetics than in other persons of the same age. Its terminal result, gangrene, was present in 6 per cent. of Joslin's fatal cases. Moreover, extreme sclerosis and gangrene, while rare in younger diabetics, does tend to occur somewhat earlier in life among diabetics than among others. Of 22 diabetic gangrene cases from the records of the University Hospital, the youngest was thirty-four years old, 2 were forty-eight, 1 was fifty, another fifty-two, 10 were from fifty-seven to sixty, 6 from sixty-three to seventy, and the oldest seventy-two. The fact that youthful diabetics rarely show arterial disease is not necessarily a valid argument against a diabetic etiology of arteriosclerosis. Syphilis is usually contracted in early life, yet its vascular manifestations do not tend to appear until the fifth decade. It is of interest to note that these diabetics with gangrene do not necessarily have an elevated blood-pressure. Of 9 patients of the group mentioned, in whom figures were available, 5 had a systolic reading between 110 and 140. The other 4 were 155, 160, 170, and 220, and in 3 of these there was other evidence pointing to chronic nephritis. The sclerotic process it seems does not necessarily involve the renal vessels. In our patient the blood-pressure was not elevated, the urine, after the disappearance of glycosuria, showed a variable specific gravity, and occasionally traces of albumin and casts, while

[1] Treatment of Diabetes Mellitus, Lea & Febiger, Philadelphia, 1917, p. 413.

the renal threshold for glucose was normal, being little under 0.172 per cent. In addition to the absence of renal sclerosis, the presence of coronary arterial disease with chronic myocardial weakness may be a determining factor of a normal or low blood-pressure in these patients.

In regard to the treatment of diabetic gangrene I wish to present just three thoughts. Too little attention is paid to prophylaxis. Elderly diabetics should be told to take regular exercise, preferably walking, to promote circulation in the legs and feet. They should pay particular attention to the cleanliness of the skin and the use of hot foot-baths is to be advised. We must warn them of the potential dangers of trifling injuries, such as a corn or toe-nail cut to the point of bleeding or a blister from a tight shoe, and urge them to report promptly for treatment when such an injury occurs. In the presence of gangrene and when amputation has been decided upon, it must be remembered that the underlying vascular disease is extensive, and that it is of a severe degree a considerable distance above the level of actual gangrene. The posterior tibial artery when dissected from the amputated leg of our patient was as hard and rigid as the proverbial pipe-stem, and broke with a crack when it was bent. Low amputation, therefore, is apt to be followed by poor healing, infection, or local recurrence of gangrene. Finally, ether and chloroform anesthesia are contraindicated. Nitrous-oxid-oxygen or spinal anesthesia should be used.

CASE II

The work of Newburgh and Marsh on high-fat feeding has been of undoubted value in pointing out to us the extent to which fats may be used to raise the caloric value of a diet to a level sufficient for maintenance and moderate activity. But high-fat feeding is a procedure that is fraught with danger. There is as yet no convincing proof that the diabetic possesses any increased power above the normal to utilize fat. It is probably also true that in diabetics and normals a certain minimal quantity of carbohydrate must be burned in order to burn at the same time a given quantity of fat: in either individual, if the carbohydrate

be lowered or the fat raised, fat combustion will no longer be complete and ketosis with acid intoxication inevitably results. If, then, a diabetic with a certain carbohydrate tolerance is utilizing the maximal amount of fat that can be completely burned under the circumstance, it is evident that the patient's margin of safety is extremely slight. Should anything occur that would suddenly impair the carbohydrate tolerance, a precipitate acidosis might result.

Catharine W., thirteen years old, developed diabetes at the age of eleven. During the first six months of illness there was no adequate diet restriction, and when admitted to the hospital in October, 1920 she was on the verge of coma. Six weeks later she was discharged in good condition with a blood-sugar of 0.130 per cent., the urine sugar free and with traces of ketones, and on a diet value of 20 calories per kilo. During the next month her diet was steadily increased until a daily carbohydrate intake of 100 grams was reached and well borne. In January, 1921, after a severe fright and nervous shock, she suffered a prompt return of glycosuria with mild acidosis, and was readmitted to the hospital. The urine was again fairly easily rendered sugar and ketone free, but the carbohydrate tolerance did not rise to its previous high level. At the end of four months it was a little less than 70 grams. When discharged in May, 1921 she was taking 70 grams of protein, 50 grams of fat, and 43 grams of carbohydrate, a caloric value of 902; her weight remained constant at 25 kilos, the urine was normal, and the blood-sugar, 0.120 per cent. During the next six months she did fairly well, with occasional traces of sugar in the urine that would clear up on a "green vegetable day." Once more a fright and later a cold brought about a more severe break in carbohydrate tolerance, and she returned to the hospital on January 26, 1922. This time her condition was decidedly worse. For over two weeks her diet contained less than 15 grams of carbohydrate, around 35 grams of protein, and 21 grams of fat, a caloric value of less than 400, while on five days of the period she was starved. Yet the urine almost daily contained sugar, from traces to 15 grams, and the blood-sugar remained high. There was, however,

some improvement in the ketonuria, and it was decided to cautiously increase the fats to bring up the caloric value.

It will be seen from Table IV that a material rise in the caloric intake was achieved solely by increasing fats, and on February 27th the urine showed only a trace of sugar, no diacetic acid, and the plasma CO_2 was 62 volumes per cent. During this period the child lost 1 kilo in weight.

Let us analyze the diet figures of this day. Based on the assumption that there is a quantitative relation between the quantity of glucose oxidizing in the body and the maximum quantity of ketogenic fatty acids that can be oxidized at the same time without the appearance of acetone bodies, Woodyatt[1] has devised a formula by means of which the ketogenic and antiketogenic substances may be calculated and a safe ratio determined. All the foods in the diet except a small fraction of the proteins are utilized in the body in one of two forms: fatty acids (ketogenic) and glucose (antiketogenic). Carbohydrates are 100 per cent. antiketogenic. Fat yields 90 per cent. fatty acid (ketogenic) and 10 per cent. glycerol, utilizable as glucose (antiketogenic). Protein gives 58 per cent. glucose; the ketogenic protein fraction is uncertain, but from certain analyses of muscle it has been computed that the maximum quantity of certain amino-acids that can yield ketones is 46 per cent. The actual figure for most protein is probably lower, but this high figure is used to be on the safe side. By certain chemical computations it is shown that in order that fatty acids be completely burned the ratio of ketogenic to antiketogenic substances (K. : A.) must not exceed 1.5 : 1. Applying this formula to the diet figures of February 27th we get K. = 16.1 (0.46 P.) + 40.5 (0.90 F.) = 56.6. A. = 20.3 (0.58 P.) + 4.5 (0.10 F.) + 9 (1.00 C.) = 33.8. (If the urine contained any sugar the amount would have to be subtracted from the total, since A. represents glucose burned.) K. : A., therefore, equals 56.6 : 33.8 = 1.67, a figure greater than 1.5, and therefore the diet would be unsafe and liable to produce acidosis. The limit of error in the formula is, however, sufficiently great on the

[1] Arch. Int. Med., 1921, 28, 125.

TABLE IV

Date.	Diet in grams.				Urine.					Blood.	
	Protein.	Fat.	Carbohydrate.	Calories.	Sugar, grams.	Acetone.	Diacetic acid.	Total N.	Ketones, grams.	Sugar, per cent.	CO_2, vol. per cent.
1/27	48	30	11	456	31.9	str.+	trace−	.....	.....	.294	46
1/29	to 9.9	0.5	12.7	95	15.7	str.+	mod.+	5.9	1.49	.....	50
2/1	9.9	0.5	12.7	95	5.7	mod.+	0				
2/2	42	...	...	168	0	wk.+	0				
2/3	32	21	10	357	0	mod.+	0	.....	.....	.163	
2/5	35	21	11	393	11.4	mod.+	0				
2/9	10	0.5	15	104	5.1	wk. +	0				
2/10	35	21	23	401	11.4	wk. +	0				
2/13	30	25	9	381	str. tr.	trace	0	7.72	.....	.250	
2/15	31	33	8	453	11.5	trace	trace				
2/17	31	33	9	457	8.6	trace	0	.....	.....	.....	63
2/20	30	40	9	516	str. tr.	wk.+	0	.....	.....	.200	
2/23	30	40	9	516	str. tr.	trace	ft. tr.				
2/27	35	45	9	581	trace	wk.+	0	.....	.....	.214	62
2/28	10	0.8	8	79	0	wk.+	0				

safe side that diets with such slightly higher ratios as, for instance, in the one under discussion will still be completely and normally utilized, and the very slight ketonuria and normal plasma CO_2 on February 27th bear this out. But when the K.: A. ratio is at 1.5 or slightly more, the patient's margin of safety is correspondingly small.

On the afternoon of March 1st the child first complained of sore throat and some aching of the arms and legs, and during the night her temperature rose sharply, reaching a maximum of 103.8° F. When seen on the morning of March 2d the patient was moderately uncomfortable; the tonsils and throat were somewhat reddened, but the lungs were clear, while the temperature was falling. The report of the previous day's urine showed traces of sugar and diacetic acid.

On March 3d there was considerable clinical improvement; the throat looked better and the temperature was lower than on the day before. The urine report of the previous day showed a return of glycosuria, but apparently because of a weakly positive acetone reaction and a negative test for diacetic acid the attending physician did not change the diet. On the morning of March 4th there was seemingly continued improvement in the general condition, but the amount of sugar in the previous day's urine showed a rise to 16.5 grams. That evening there was an accession of fever. On the following day anorexia and some vomiting appeared and the respiratory rate began to rise. Active measures to check the increasing acidosis, including elimination of fat intake, with an increase in carbohydrate and fluids, the use of whisky and soda were applied, but to no avail. On March 7th, six days after the onset of the infection, the child died in coma.

Here, then, is an instance of a trivial general infection proving disastrous in a patient on a high-fat diet. The objection will, of course, be raised why was the high-fat diet not stopped at the very beginning of the infection, and the objection is an eminently proper one. It is a long-known truth that acute infectious diseases in diabetics may precipitately lower carbohydrate tolerance and thereby induce acidosis, and under these

TABLE V

Date.	Diet in grams.				Urine.					Blood.	
	Protein.	Fat.	Carbohydrate.	Calories.	Sugar, grams.	Acetone.	Diacetic acid.	Total N.	Ketones, grams.	Sugar, per cent.	CO_2, vol. per cent.
3/1	35	45	8	577	trace	mod.+	trace				
3/2	35	45	9	581	6.3	wk.+	neg.				
3/3	34	45	9	577	16.5	str.+	neg.				
3/4	35	45	8	577	+	+	+				
3/5	42	19	90+	...	36.3	str.+	neg.				
3/6	28	0	36+	...	28.9	str.+	str.+	6.29	8.49	.416	17
3/7	28	0	36+	...	+	+	+				

circumstances we must temporarily abandon all thought of treating the diabetes and center our effort on the prevention of acidosis. But the fact remains that a previous high-fat diet rendered our patient more vulnerable. Now, from the standpoint of the practitioner, if the above events could take place in a well-equipped modern clinic, how much more likely could they do so in private practice when it might be several days before the patient with a "cold" or "sore throat" thought it worth while to report to his doctor? Moreover, the so-called high-fat diet our patient was receiving was not particularly high as those diets go. Its fatty acid-glucose ratio was 1.67 (this figure, of course, rose as soon as sugar appeared in the urine). Of the diets given by Newburgh and Marsh to their patients not a few had ratios well over 2. High-fat feeding has certain advantages, but it also has very real dangers that must make us pause before an unqualified acceptance of high-fat feeding, and when for one reason or another we must to some degree resort to it, the possible dangers should constantly be uppermost in our minds.

CLINIC OF DR. EDWARD WEISS

JEFFERSON MEDICAL COLLEGE

PROFUSE HEMOPTYSIS

Case I. Fatal Pulmonary Hemorrhage in a Case of Mitral Stenosis.

Case II. Severe Pulmonary Hemorrhages in a Tuberculous Patient with Chronic Valvular Disease.

GENTLEMEN: I wish to speak to you today of 2 patients who had profuse pulmonary hemorrhages, the one of mitral stenotic origin, the other in a patient with aortic and mitral valvular disease, but in whom the hemorrhages were probably due to tuberculosis.

CASE I

I. G., an adult, white male, aged twenty-five years, who was admitted to the service of Dr. S. Solis Cohen on April 16, 1922, complained of shortness of breath and cough upon the least exertion. His family history was good. He had always been in good health and did not recall the diseases of childhood. He had influenza in 1920.

Present Illness.—One year ago the patient gave up work because of marked cough and dyspnea on slight exertion. This has progressively increased since, although there have been a few periods of a week or two during which time he has been partially relieved of symptoms. He has a moderate amount of expectoration, which is frequently blood-streaked, and has frequent night-sweats. For the past year he has had precordial pain. In the last two days the patient has had frank hemoptysis on three occasions, losing from 4 to 8 ounces of blood at a time. The main points in the physical examination follow:

The patient is a fairly well-nourished adult white male with considerable dyspnea and cyanosis. Temperature on admission 101° F., pulse 140, respirations 50. Expansion is full and equal. On palpation there is marked bronchial fremitus over the entire chest, which is resonant throughout. Many moist râles are heard throughout the chest, especially on the right side. The quality of the breath sounds is obscured.

Heart.—The apex-beat is difficult to localize; there is a normal area of cardiac dulness. A diastolic thrill is felt and, on auscultation, a distinct presystolic murmur is heard in a limited area just to the right of the nipple.

Progress.—The day after admission the patient's general condition was poor; he was delirious at times and had rather profuse hemorrhages, losing from 6 to 8 ounces of blood at a time. This condition continued for the next two days. On May 20th his general condition was somewhat improved; blood-spitting seemed to have been controlled by horse-serum. The following day (May 21st) the patient seemed improved in spite of the fact that he had lost a pint of blood during the night. On the 22d the patient was still bleeding profusely and showed marked evidences of the loss of blood; later the same day he developed pulmonary edema and died.

On admission the hemoglobin was 80 per cent., red blood-cells 4,470,000, white blood-cells 17,000. The hemoglobin progressively diminished, and on the day of his death was 46 per cent. Four sputum examinations were negative for the tubercle bacillus. The urine was negative; the blood Wassermann was positive, +1.

The following notes are taken from the necropsy record:

The body is that of a young adult white male, considerably emaciated, approximate weight 125 pounds. There is clotted blood in the mouth and nostrils. A persistent thymus weighing 45 grams overlies the upper surface of the pericardium. About the trachea, at the bifurcation, are some enlarged, firm, yellowish-red lymph-nodes weighing collectively 40 grams.

The left lung is large and voluminous; the pleural cavity contains no fluid; there is one small, readily broken adhesion

at the apex. The lung is pinkish-red in color; the lower lobe is considerably enlarged and has a yellowish tinge. It has a curious doughy feel. The tissue pits, but contains air throughout. On section, the upper lobe is dark red, tissue is fairly firm, and yet partially crepitant. The lower lobe retracts on incision and is quite edematous. The incised surface of the upper lobe is comparatively dry, and the cut ends of the vessels and bronchi show plugs of clotted blood.

The right lung is very large, all of the lobes being proportionately enlarged. The tissue is partially crepitant, and upon section shows about the same changes as have been described in the left lung. Like its fellow, it shows no evidence of consolidation or tuberculosis.

The heart appears slightly enlarged, and, on section, the left ventricular muscle is found to be 1.5 cm. in thickness and dark red in color. The aortic cusps show adhesions and calcific deposits, and narrowing of the orifice. The mitral area is markedly diseased. The orifice is much narrowed and the cusps stiffened, fibrosed, and calcific. An ulcerative area extends from the posterior surface of the orifice into the auricle. The left auricle is hypertrophied and distended with blood-clot; the right ventricle is hypertrophied; the wall is 0.75 cm. in thickness. The right auricle is similarly hypertrophied and distended with blood-clot, but the tricuspid orifice appears competent. This is taken as proof that the congestion was practically limited to the lungs, for the abdominal organs show no marked evidence of passive congestion.

The gross diagnoses were: Chronic valvulitis (aortic and mitral), with mitral stenosis, hypertrophy and dilatation of the left auricle, right ventricle, and right auricle. Lungs: Passive congestion (brown induration) and edema; compensatory emphysema. Persistent thymus. Hyperplasia of the peritracheal nodes and of the lymphoid follicles of the spleen. The histologic examination confirmed these findings.

As you well know, hemoptysis is a very frequent symptom in mitral stenosis; indeed, cough and hemoptysis may be the earliest symptoms; and for the reason that these symptoms

occur in individuals who present confusing pulmonary signs, they are frequently thought to be of tuberculous origin, because of a failure to appreciate the cardiac lesion. In this patient the diagnosis was even more difficult than it usually is because of the profuse pulmonary hemorrhage; that is to say, there was no question about the presence of mitral stenosis, but it was doubtful whether or not tuberculosis was also present to account for the profuse and fatal hemorrhages. The necropsy as noted above confirmed the cardiac findings and showed that pulmonary tuberculosis was not present; merely a brown induration which accompanies advanced cardiac disease with decompensation.

This, then, may be put down as an unusual case of fatal pulmonary hemorrhage of mitral stenotic origin.

CASE II

A short time after the death of the patient whose history has just been related another patient with profuse pulmonary hemorrhage was admitted to the ward. His history follows:

T. B., an adult white male, aged thirty-five years, who was admitted to the service of Dr. S. Solis Cohen on May 15, 1922, gave a history of repeated hemorrhages by mouth. His family history is good.

Past History.—He does not recall the diseases of early life, but had an attack of rheumatic fever at the age of twenty-four, which confined him to bed for six weeks. Two years later he had a second attack. He had gonorrhea at the age of twenty-nine, but denies syphilis. He had always been in good health until the onset of hemoptysis about six years ago. At that time, while walking on the street, his mouth filled with blood. The hemorrhage continued the entire day, and he states that about 1 pint of blood was lost. One year later hemorrhage recurred, and again he lost about 1 pint of blood. In 1918 the patient had a severe attack of influenza. During this illness hemoptysis recurred over a period of six days, with from ten to twelve hemorrhages daily. At the onset of this illness his weight was 175 pounds; at the termination, 125 pounds. Since

then from time to time his sputum has been blood-streaked, and he has had dyspnea upon exertion, especially upon climbing stairs. He has, however, regained his weight, has had no night-sweats, but is subject to colds in the winter-time. His appetite is good.

Present Illness.—Upon wakening the morning of May 14th the patient felt a small amount of blood in his mouth. He arose, dressed, and went to work, but soon after reaching his place of employment the hemorrhage recurred and he returned home and went to bed. That day he had six or seven hemorrhages, losing about 1 quart of blood. The following day he had three hemorrhages during the morning, and two smaller ones in the afternoon after reaching the hospital. This morning (May 16th) the patient has had several hemorrhages, losing about 1 pint of blood. The main features of the physical examination follow:

The patient is a pale, fairly well-nourished white male adult. His chest is well developed; expansion appears full and equal, but there is impaired resonance below the right clavicle. There are scattered râles on both sides of the chest over the apices and in the first and second interspaces.

Heart.—The apex-beat is in the fifth interspace just outside the nipple line. On palpation there is both a systolic and a diastolic thrill over the region of the second right interspace, and the systolic thrill is transmitted into the vessels of the neck. There is a typical Corrigan and capillary pulse, and a nodding of the head with systole. A double murmur is heard in the aortic area; the systolic is transmitted into the vessels of the neck and the diastolic down the right border of the sternum. In addition, there is a double murmur at the apex.

On admission to the hospital the temperature was subnormal, pulse 120, respiration 24. The systolic blood-pressure was 160, diastolic 40.

The patient continued to bleed after admission to the hospital, and by the evening of the 16th had lost about 1 quart of blood. His hemoglobin was reduced to 65 per cent. By the 17th the bleeding was controlled, following the administration

of horse-serum, and his general condition was satisfactory. His improvement continued, and except for a serum reaction with profuse eruption, pain in the joints, elevation of temperature, pulse-rate, and respiration, he continued to improve and was discharged on June 15th. The first three days in the hospital his sputum was negative for tubercle bacilli, but after that was repeatedly positive. The *x*-ray examination disclosed the heart considerably enlarged, especially the left ventricle; the position was almost transverse; and the entire aortic arch was dilated to a considerable degree. About a week before his discharge the *x*-ray examination of his chest revealed marked thickening at the roots of both lungs, old tuberculous deposits in both apices, and a probable cavity in the right apex, with more recent and more extensive infiltration of the middle lobe on the right side, and to a lesser extent of the lower lobe on the left side. The electrocardiographic examination showed a rate of 85, with regular rhythm, left ventricular hypertrophy, and myocordial degeneration.

Having learned a lesson in the previous case, we were for a time doubtful of the presence of tuberculosis in this patient, who presented undoubted signs of cardiac disease. Even after confirmation by the *x*-ray and sputum examinations, we were still in some doubt as to the origin of the pulmonary hemorrhage. In the presence of both lesions, however, it is probably safer to ascribe the hemorrhage to the tuberculosis; and the fact that the patient is alive and in fairly good health today (six months later) makes this the more probable supposition.

The lesson to be learned from the study of these cases is an old one, but none the less important and necessary to reemphasize; that is, the necessity for careful examination of the heart in patients who complain of cough, dyspnea, and hemoptysis. In addition, there is still the further necessity in such cases, once it has been established that cardiac disease is present, to exclude the possibility of a concomitant pulmonary tuberculosis.

CLINIC OF DR. BAXTER L. CRAWFORD

JEFFERSON HOSPITAL (DEPARTMENT OF PATHOLOGY)

CASE OF TUBERCULOUS EPIDIDYMITIS TERMINATING IN TUBERCULOUS MENINGITIS PRODUCING XANTHOCHROMIA OF THE SPINAL FLUID

W. R. White male aged sixty-five; carpenter; admitted to service of Prof. H. A. Hare May 20, 1922.

Chief Complaint.—Pain and swelling of left ankle, with pain in left shoulder.

Family History.—Negative.

Personal History.—Patient states that he had measles in early childhood. No other infectious diseases except influenza during an epidemic at about the age of thirty. There was no history of venereal disease.

Present Illness.—Began one month ago with pain and swelling in left ankle. One week later noticed pain in left shoulder and upper part of spine, slight occasional pains in other joints.

Physical Examination.—Patient is a fairly healthy looking white male. No evidence of dyspnea or cyanosis. Walks with a limp, favoring the left foot. The left ankle is enlarged and tender to pressure, but not reddened or warm to touch.

Special examination of teeth, tonsils, and sinuses to find any possible foci of infection were negative with exception of tonsils, which were not particularly enlarged, but considered to be diseased. Patient gave no history of trouble with testicles, but, on examination, the left epididymis was found to be enlarged and indurated. The right lobe of the prostate was also enlarged and nodular, but not tender. Examination of chest and abdomen negative.

On admission the temperature ranged from normal or slightly above, in the morning, to 100° to 101° F. in the afternoon. Pulse 80/90. Respiration normal. Blood count: Hemoglobin,

87 per cent., Red cells, 4,780,000; white cells, 6000; color index, 0.9. Urinalysis showed a faint trace of albumin, otherwise negative. Blood Wassermann negative. Blood-culture was sterile.

After a short time of rest in bed, with local and general treatment, the arthritis improved, but the patient continued to run a temperature frequently as high as 102° F., which could not be accounted for, and his general condition became gradually worse. Later urinalysis showed a trace of albumin, a few pus-cells, and an occasional hyaline cast. The leukocyte count was 4200. Widal negative and second blood-culture was also sterile.

The enlarged testicle became slightly painful, but this was considered to be due to slight trauma.

About July 4th, six weeks after admission to ward, patient began to show cerebral symptoms, such as slight mental confusion and stupor, with occasional muscular twitching. Repeated urinalyses showed a trace of albumin, many pus-cells, and an occasional hyaline cast. July 5th lumbar puncture was performed, and a clear, light canary yellow colored fluid was obtained. Examination of the fluid showed the following findings: 147 cells per c.mm.; globulin markedly increased; copper solution reduced; Wassermann negative. A slight coagulum formed in the fluid on standing. Smears were negative for acid-fast bacilli and cultures failed to reveal any growth.

The mental condition and stupor of the patient increased. Muscular twitching became more marked, and when one of the extremities was moved patient would cry out with pain. There was no paralysis. The clinical manifestations pointed to encephalitis, while the spinal fluid findings indicated pressure on the cord, with chronic meningitis, probably tuberculous.

A second lumbar puncture performed a day or so later showed the fluid to be a deep yellow color, with other findings similar to previous examination. Patient died July 13, 1922.

No. 14,475. Autopsy twenty-eight hours after death.

Body is that of an adult white male, well developed but considerably emaciated. Hair is scanty. Eyes negative; pupils

slightly dilated, but equal. A number of teeth are absent; gums are shrunken. No enlarged lymph-nodes. Chest is negative. Abdomen is flat. No edema of extremities. No perceptible enlargement or inflammation of joints. On section, the subcutaneous and omental fat is scanty.

Peritoneum.—Cavity contains practically no fluid. Intestines are markedly distended with gas. Organs occupy their normal relations. The visceral peritoneum and surface of mesentery present a few pin-head foci, rather firm and sharply circumscribed. No enlargement of lymph-nodes.

Pleuræ.—Left side is free from fluid and adhesions. On surface of visceral pleura are numerous very fine white foci. Right cavity is obliterated by dense adhesions around the apex and over the posterior surface of upper and lower lobes. No fluid. Tiny foci are also seen on the visceral surface.

Pericardium appears normal. *Heart* weighs 320 gm. Muscle is soft and there is a considerable amount of subepicardial fat. The vessels are tortuous. On section, the heart muscle is pale. Right side appears normal. Left auricle and ventricle are about normal in size. Mitral and aortic cusps are slightly thickened and fibrosed. Coronaries are slighlty sclerotic.

Lungs.—Left weighs 750 gm. It is fairly well aërated, with the exception of dependent portion of lower lobe, which is tough and contains small nodules. Incised surface of the dependent portion is deep red and mottled. Pus exudes from the bronchi in lower lobe. In the substance of the upper lobe are a few shot-like calcified bodies and a few tiny gray foci. Peribronchial lymph-nodes are enlarged and anthracotic, but no calcified areas are observed. Right lung weighs 670 gm., and crepitates throughout. Dependent portion of both upper and lower lobes is tough and nodular. On section this part of the lung is deep red and mottled, and contains a few small dark gray foci similar to those described in left. A number of the peribronchial lymph-nodes on this side are enlarged and anthracotic. One large node contains several calcific areas.

Spleen weighs 170 gm., and is soft in consistency. Incised surface is deep red; follicles are indistinct.

Adrenals appear normal.

Kidneys.—Left weighs 170 gm., is rather soft. Capsule strips readily, leaving a fairly smooth surface. Relation between cortex and medulla is normal. Right kidney weighs 160 gm., and presents same appearance as opposite organ.

Bladder is markedly distended with cloudy urine. The wall is thickened, trabeculæ are hypertrophied, mucosa is red.

Prostate is enlarged and irregular; right lobe is markedly enlarged, smooth, and firm. Incised surface of right lobe contains a number of circumscribed caseous areas. The left lobe, on incision, appears to be normal. There is considerable fluid around the left testicle. Left epididymis is enlarged and indurated, and, on section, caseous material escapes. The testicle is rather small, but otherwise appears normal. Right testicle and epididymis shows no macroscopic change.

Gastro-intestinal Tract.—Stomach and intestines, no macroscopic change.

Liver weighs 1350 gm., is soft in consistency. Incised surface is red and dark brown. Blood-vessels are engorged, markings are indistinct. *Gall-bladder* is normal.

Pancreas weighs 130 gm., and appears normal.

Aorta shows a slight thickening with atheroma of the intima. The small vessels are also slightly sclerosed.

Brain weighs 1455 gm. Scalp and calvarium appear normal. Dura is distinctly adherent to inner surface of the skull. The pia arachnoid contains a considerable amount of clear serous fluid. Blood-vessels are slightly injected, but there is no perceptible inflammation of the meninges over the brain. No evidence of foci in the meninges. Section of the brain reveals no gross lesion. The ventricles are not dilated.

Cord.—On splitting the dura a thick yellowish exudate is found in the pia arachnoid in thoracic and lumbar regions. The exudate is sharply circumscribed in upper thoracic region. The superficial vessels are injected and a few small whitish foci appear on the surface of the meninges. Bodies of the vertebræ appear normal.

Gross Diagnosis.—Tuberculous meningitis, localized, thoracic

and lumbar portions of cord. Tuberculous epididymitis, left. Tuberculosis of prostate, right lobe. Miliary tuberculosis of peritoneum, pleura, and both lungs. Bronchopneumonia, diffuse bilateral. Chronic adhesive pleuritis, right. Marked anthracosis of lungs.

Histologic Diagnosis.—Chronic fibrocaseous tuberculosis of prostate. Acute miliary tuberculosis of lungs, liver, spleen, kidneys, and peritoneum. Early bronchopneumonia. Pulmonary congestion.

Bacteriology.—Smears from the meninges of the cord and left epididymis show a number of acid-fast bacilli. Cultures from heart's blood remain sterile.

A retrospective study of the case reveals a number of points of interest. The rapidly and widely disseminated tuberculous infection, originating in the focus in the epididymis, the extensive tuberculous lesion in the prostste, the indefinite clinical symptoms pointing to a probable encephalitis rather than meningitis, the localized meningitis confined to the cord, producing the xanthochromic spinal fluid. Tuberculous epididymitis is too frequently looked upon as purely a local lesion, while, in reality, the danger always exists of a rapid spread of infection from this site to other organs, as happened in this case. At the autopsy a careful search was made for other foci of tuberculous infection, but none could be found.

The phenomenon known as xanthochromia of the spinal fluid was first described by Froin in 1903,[1] and at first was considered pathognomonic of pressure on the cord, but in a number of instances, as in this case, no direct pressure on the cord was found. However, there seems to be no doubt in every case the free circulation of the spinal fluid is interfered with by either intradural exudate or by direct pressure. The yellow coloring-matter is considered to be derived in some way from the blood, but just how it is produced has never been satisfactorily explained.

[1] William Boyd, Physiology and Pathology of the Cerebrospinal Fluid, The Macmillan Co., New York, 1920.

CLINIC OF DR. LEON JONAS

WOODWARD FELLOW IN PHYSIOLOGIC CHEMISTRY, PEPPER LABORATORY, UNIVERSITY OF PENNSYLVANIA

RENAL GLYCOSURIA

RENAL glycosuria has been considered a rare condition, but in the last five or six years the literature has contained the reports of numerous cases. This entity most probably occurs more frequently than has heretofore been supposed, but has failed of recognition.

The first case of renal glycosuria was reported by Klemperer in 1896, and from that time until 1918 not more than two dozen cases have been recorded in the medical literature.

The introduction of microchemical methods, because of the small quantity of blood required and because of the simplicity, and at the same time accuracy of these methods, has made it much easier to diagnose this condition.

The cardinal signs which distinguish this type of glycosuria from the glycosuria due to other causes are:

1. Glycosuria practically uninfluenced by diet.
2. A normal blood-sugar concentration or a tendency to hypoglycemia.
3. The disappearance of the glycosuria occurs if the permeability of the kidneys becomes impaired as in nephritis.
4. The absence of the symptoms of diabetes mellitus.
5. Klemperer's case and a few of the other early cases had an accompanying albuminuria.

Some of the more recently reported cases have shown a variance from the above symptoms, as is illustrated by Group 3 in the following classification. The cases of renal glycosuria may be classified into three groups:

Group 1. This group includes those cases which exhibit a very mild glycosuria, usually less than 10 gm. per day. The

glycosuria is unaffected by diet. The fasting blood-sugar concentration is normal, and the curve after giving 100 grams of glucose by mouth is also normal. The symptoms of diabetes mellitus are absent.

Group 2. The cases in this group show the same symptoms enumerated under Group 1, with the addition of an albuminuria.

Group 3. In this class are grouped those cases in which the glycosuria may vary from 20 to 40 or more grams per day, with a concentration in the urine as high as 5 per cent. or above. The glycosuria is influenced by diet. The fasting blood-sugar concentration is normal, but after feeding 100 grams of glucose by mouth it may reach a height considerably above normal.

The usual history of most cases of renal glycosuria is that sugar was found in the urine in a life insurance examination or in a routine examination during an illness entirely independent or unrelated to this condition.

The first case reported in this paper is representative of Group 3.

Case I.—A white American male aged twenty-four admitted to the service of Dr. Alfred Stengel at the Hospital of the University of Pennsylvania May 3, 1921 because of painful urination and headache. In November, 1918, while on duty in the United States Navy, he reported to the sick bay because he had fainted on the day previous for no apparent reason. The routine examination of the urine revealed the presence of sugar. He was then sent to the Brooklyn Naval Hospital for treatment. The patient did not have an excessive thirst or polyuria at any time. His appetite was always good and there had been no loss of weight. He was discharged from the Navy in February, 1919, and states that he had not been sugar free up to that time.

On returning to his home his physician placed him on a restricted carbohydrate diet. On this diet he claims that at times he was sugar free. He entered the University of Pennsylvania as a student in September, 1920, and since then he has partaken very freely of carbohydrates, such as bread, cereals,

etc. During the month previous to his admission to the hospital he suffered from paresthesias of the lower limbs, frequent headaches, and frequency and difficulty in voiding urine. Only a small quantity of urine was voided during the act of urination. He has not had any polyuria or thirst.

His past medical history is negative except for mumps in his sixth year and measles during the eighth.

Physical Examination.—The patient was of short stature, with an excellent development and good musculature. There was a slight odor of acetone on his breath. His tongue was slightly reddened. The genitalia were negative. His gait and station were normal, as were the reflexes and sensation. Blood-pressure on admission was systolic 118, diastolic 60. Physical examination was negative otherwise. *x*-Ray of the sella turcica was negative.

Laboratory Examination.—The urine in the morning after admission was clear, acid, amber color, specific gravity 1039, trace of albumin, occasional hyaline and granular casts, 1.5 per cent. sugar, trace of acetone, no diacetic acid. All subsequent examinations of the urine were negative for albumin and casts. The urine fermented with yeast. The blood count was as follows:

Erythrocytes 5,100,000, leukocytes 8200, hemoglobin 101 per cent. The differential count: Polymorphonuclears 74 per cent., lymphocytes 18 per cent., large mononuclears 5 per cent., transitionals, 3 per cent.

The phenolsulphonephthalein elimination after the intravenous injection of the dye was 85 per cent. in two hours.

On May 4th the chemical examination of the blood revealed the following:

Blood urea nitrogen 21 mg. per 100 c.c., plasma carbon dioxid capacity 57 volumes per cent. The fasting blood-sugar concentration on May 5th was 0.072 per cent. The blood urea nitrogen on May 21st was 18 mg. per 100 c.c. Wassermann was negative.

The daily intake of food and the results of laboratory examinations are found in Table I (p. 1082).

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TABLE I

Date.	Food.				Urine.						
	Protein, gm.	Fat, gm.	Carbohydrate, gm.	Calories.	Amount, c.c.	Reaction.	Specific gravity.	Glucose, gm.	Acetone.	Diacetic acid.	Total N., gm.
5/4/21	Light diet.			...	....	Acid.	1039	....	0	0	
5	68	52	13	782	1150	"	1025	29.5	x	0	
6	68	52	18	812	1960	"	1027	51.5	xx	x	
7	68	52	15	800	2230	"	1028	46.4	xx	x	
8	74	56	15	860	610	"	1030	....	xx	x	
9	74	56	15	860	1490	"	1032	43.8	xx	0	
10	83	59	17	931	2040	"	1024	36.2	xx	x	
11	84	59	17	935	2030	"	1024	43.6	xx	x	
12	83	59	17	931	1125	"	1030	28.4	xxx	xx	
13	83	59	21	947	2010	"	1026	62.0	xxx	xx	26.9
14	82	59	17	927	1100	"	1031	28.7	xx	x	
15	83	59	17	931	1120	"	1030	24.0	xx	0	
16	99	59	15	987	1105	"	1028	29.0	xxx	x	
17	99	52	14	920	2470	"	1034	75.9	xx	x	
18	106	50	16	938	2010	"	1028	48.6	xx	x	
19	106	50	16	938	1715	"	1034	59.9	xxx	xx	
20	106	50	16	938	1875	"	1035	59.1	xxx	xx	25.1
21	Starvation.				1565	"	1028	32.8	xx	x	
22	100	50	16	914	1620	"	1028	28.0	xx	x	15.25
23	100	50	16	914	1750	"	1016	40.2	xx	x	17.45

x equals Trace.
xx equals Moderate amount.
xxx equals Large amount.

On May 7th the blood-sugar tolerance after taking 75 gm. of glucose by mouth was as follows:

	Blood-sugar per cent.	Percentage of glucose in urine.
¾ hour after glucose	0.15	3.0
1¾ hours after glucose	0.18	3.7
2¾ hours after glucose	0.147	6.5
3¾ hours after glucose	0.092	5.8

Unfortunately, the fasting blood-sugar specimen was lost.

Discussion.—It must be admitted that there are features in this case that resemble diabetes mellitus, particularly the tendency to ketonuria, and the marked effect of the carbohydrate intake on the glycosuria. On the other hand, the very low threshold for glucose may account for these findings. The low threshold is proved by the presence of a glycosuria coincident with the low blood-sugar as is revealed by the following experiment: No food was taken after 4 P. M. At 2 A. M. the next morning he emptied his bladder, and a specimen of urine was collected from this time until 9 A. M., when a venous puncture was made for the blood-sugar determination. The blood-sugar

concentration was 0.069 per cent., while the urine specimen contained 2.3 per cent. glucose.

On May 5th, after a carefully controlled fast of thirty-six hours, the starvation level of the blood-sugar was 0.06 per cent., while the urine voided at the same time that the blood was collected contained 2.1 per cent. glucose. The patient had voided two hours before this specimen of urine was collected.

The blood-sugar curve following the ingestion of 75 gm. of glucose can hardly be considered abnormal except possibly the delay in the return to base line. It is known that after starvation the response of the body to carbohydrate is toward hyperglycemia. The peak at 0.189 per cent. could be caused by the very limited diet, which was especially low in carbohydrate.

The occurrence of the ketonuria may be explained by the low caloric intake, particularly of carbohydrate, which together with the marked loss of glucose in the urine has brought about a state of starvation; in other words, it was a starvation ketonuria. The other possible cause for the ketonuria is a limited tolerance for carbohydrate. If the latter cause is correct then we have a combination of renal glycosuria and diabetis mellitus. If the former is correct, the ketonuria should disappear when the patient is placed on a full unrestricted diet.

The destruction of endogenous protein evidenced by the great nitrogen loss as shown by the excess of urinary nitrogen over the intake of nitrogen is due to two factors. The caloric intake is insufficient for the body needs, and as a result the body breaks down its own protein to make up the deficit, and since 58 per cent. of the protein molecule is convertible into glucose, and a large part of this glucose is lost by its escape into the urine, it is evident that more protein must be destroyed to supply a given amount of energy than would be the case in a normal organism. In this respect the case simulates experimental diabetes produced in animals by phloridzin, although it is stated by some authorities that phloridzin, in addition to causing a glycosuria, inhibits the oxidation of glucose.

As stated above, the question to be settled in this case is whether this is an uncomplicated case of renal glycosuria, the

low threshold for glucose causing all the symptoms, or is it a case of renal glycosuria with diabetes mellitus? With the data at hand it is realized that this question cannot be definitely decided. It is hoped that at some future time we will be able to persuade this patient to return to the hospital for further study of the respiratory quotient and a more intensive study of the dextrose-nitrogen ratio.

In a letter dated September 24, 1922 the patient states that his last blood-sugar was below normal as usual. A twenty-four-hour specimen showed 2 per cent. sugar. These tests had been made once a month. He states that his general condition is very satisfactory, and that he is able to participate in various activities which require more than the usual amount of exertion. The urine is free of acetone and diacetic acid. He states that he is on a restricted diet as far as starches are concerned. He has used milk during the past few months, but his chief source of food has been meat.

The second patient to be reported is an example of a low threshold for glucose in which the glycosuria is only occasional. The history of the case is as follows:

Case II.—H. L., white male Russian Hebrew, aged twenty-seven years, was admitted to the service of Dr. Alfred Stengel at the Hospital of the University of Pennsylvania September 14, 1922 because of polyuria, polydipsia, and the symptoms of a sexual neurosis.

A year and a half ago he noticed that he voided more urine than usual without any urinary discomfort. This condition has continued periodically up to the present time. He has had no marked increase in appetite and has lost no weight. Two weeks before admission to the hospital his physicain discovereed sugar in the urine. He is unmarried and has a comfortable home. His occupation is that of a barber. His father died of diabetes.

Physical Examination.—The blood-pressure was systolic 120, diastolic 90. Patient is a well-nourished young adult with good muscular development, weighing 74 kilograms. The physical examination is negative.

On cystoscopic examination the findings are as follows: The patient has an enormous verumontanum and a highly injected trigone. Both are probably the results of masturbation. The cystoscopist state that the patient has formed a habit of voiding on the first bladder sensation which, in turn, has resulted in reducing the carrying capacity of his bladder with comfort to about 2.5 ounces. This has eventually made it necessary for him to rise at night.

Laboratory Examinations.—The Wassermann was negative. The blood-count revealed 4,910,000 erythrocytes, 12,000 leukocytes, 89 per cent. hemoglobin, and a differential count as follows: Neutrophils 71 per cent., lymphocytes 21 per cent., large mononuclears 5 per cent., transitionals 2 per cent., eosinophils 1 per cent. Urine examination of a single voiding on admission was amber color, acid reaction, specific gravity 1032, albumin and sugar negative. The microscope revealed much mucus and a few white blood-cells. The subsequent urinalyses were negative for glucose except when the sugar tolerance tests were made. The fasting blood-sugar level on September 18th was 0.081 per cent.

Because of the history of glycosuria it was decided to test his sugar tolerance by giving 1.8 grams of glucose for each kilo of body weight. The results of this test are given in the following table:

	Blood-sugar per cent.	Amount of urine, c.c.	Glucose.
Fasting	0.079	25	Absent
½ hour after glucose	0.113		
1½ hours after glucose	0.081	35	Trace
2½ hours after glucose	0.061	65	0.78 gram

Because of the presence of glucose in the urine and the low blood-sugar concentration it was thought that possibly the peak of the blood-sugar concentration had been missed, because the intervals between the examinations were too great, and, consequently, it was decided to repeat this test, taking specimens of blood at fifteen-minute intervals. The results of this test are as follows:

	Blood-sugar, per cent.	Urine: Amount, c.c.	Glucose, gm.	Glucose, per cent.
After breakfast	0.101	20		
15 minutes after glucose	0.101			
30 minutes after glucose	0.125	40	.77	1.9
45 minutes after glucose	0.111			
60 minutes after glucose	0.088	22	.66	3.0
75 minutes after glucose	0.087			
90 minutes after glucose	0.091	38	.20	0.5
2½ hours after glucose	0.075	285	Trace	

Discussion.—This patient represents a type of glycosuria due to a low threshold for glucose apparently between the blood-sugar concentrations 0.11 and 0.125 per cent. As a result of this definite threshold, the glycosuria in this case can be influenced by diet.

This case is not presented as one of renal glycosuria in the strict sense because it is obvious that the presence of the glycosuria depends on the carbohydrate intake, and then only after a large amount has been taken, but nevertheless one is justified in calling this a type of renal glycosuria. The apparent paradox of a low glucose threshold and the presence of a glycosuria only after taking a very large quantity of carbohydrate is due to the very marked tolerance for carbohydrate which this patient fortunately enjoys.

Whether the marked tolerance for glucose in the presence of the low threshold is a compensatory mechanism or a happy coincidence must remain unsolved. The lesson from this case is that there is a patient with a diagnosis of diabetes mellitus, who, to the contrary, not only has not diabetes mellitus, but an unusually good tolerance for carbohydrate as is shown by the sugar tolerance tests.

Prognosis and Treatment.—The recognition of renal glycosuria is of utmost importance from the standpoint of prognosis and treatment. Diabetes mellitus is a serious condition with a grave outlook, while renal glycosuria is an anomaly which, it is supposed, does not influence the health of an individual. This statement concerning renal glycosuria is given with a reserve because the cases reported have not been followed long

enough as a group to permit an accurate deduction to be made as to the ultimate influence of this condition on the health of the patient. A few cases have been reported in which the glycosuria has continued for many years without apparently undermining the health of the patient.

The treatment in any case of glycosuria should not be outlined until the cause of the glycosuria is known. If it is renal in origin it is believed at the present time that dieting is unnecessary. If due to diabetes mellitus, fasting and restriction of diet are the all-essential things in so far as the dietary treatment is concerned. As many cases of renal glycosuria continue to have glucose in the urine in spite of long fasts because of the great permeability of the kidneys for glucose, it is evident that nothing beneficial is accomplished by fasting, but, indeed, much harm is brought about because of the loss of weight and strength. This is very well illustrated by our attempt to restrict the diet in the first patient reported in this paper. From these statements it is manifest that the treatment for diabetes mellitus is contraindicated in renal glycosuria, and vice versa.

Finally, a diagnosis should never be made in a case of glycosuria until blood-sugar tests have been done, for it is only by this procedure that an accurate diagnosis can be made and appropriate treatment outlined.

Patient No. 1 presented himself at the clinic after this paper had been sent to the press. He appeared to be in very good health. His blood-sugar concentration one hour after a breakfast consisting of cereal, etc., was 0.082 per cent., while a specimen of urine voided immediately after the venous puncture contained 2.5 per cent. of glucose and was free of acetone and diacetic acid.

CONTRIBUTION BY DR. HAROLD W. JONES

DEPARTMENT OF MEDICINE, JEFFERSON MEDICAL COLLEGE HOSPITAL

PIGMENT METABOLISM AND THE VAN DEN BERGH TEST TO DIFFERENTIATE OBSTRUCTIVE AND NON-OBSTRUCTIVE JAUNDICE; WITH FIVE CASE REPORTS

THE entire subject of pigment metabolism is still one concerning which there are many disputed points. The literature is full of assertions and contradictions concerning the origin, the relation between, and the ultimate distribution of the various body pigments. However, much that is theoretic can be eliminated and certain facts set out upon which the majority of the workers seem to agree.

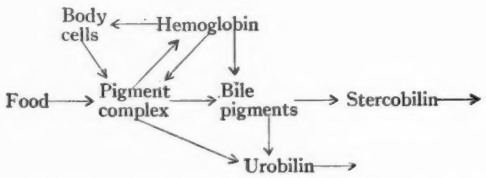
The older conception of pigment metabolism is that certain foods and iron are utilized in the bone-marrow to form hemoglobin, and that when the red cells are destroyed the hemoglobin is liberated and reduced in the liver value for value. These bile pigments are reduced in the intestine to stercobilin, of which a large portion is excreted in the feces, but a certain amount is reabsorbed and re-excreted by the liver. If the liver is not functioning normally this material may escape the portal system and is excreted as urobilin by the kidneys.

More recent investigators[1] advanced the theory that the stercobilin reabsorbed from the intestine was resynthesized to form new hemoglobin. This assumption, however, has been disproved, and it has been definitely shown that stercobilin is not reabsorbed from the intestine or resynthetized to form hemoglobin. The stercobilin is formed from the bile pigment by the action of bacteria, and the amount of stercobilin is influenced

[1] Wilbur and Addis: Arch. Int. Med., 13, 235, February, 1914.

greatly by the type of diet and amount of destruction of body protein.

These investigators[1] further postulate the presence of a pigment complex, an intermediary substance which is constructed from the food, from the body cells, and from the liberated hemoglobin; and from which, in turn, may be formed hemoglobin, bile pigments, urochrome, and urobilin. They further show that body cells may form hemoglobin through the medium of the pigment complex, that food may form hemoglobin in the same manner, and that between the liberated hemoglobin and the pigment complex there is a reverse reaction; that is, liberated, hemoglobin goes to make up the pigment complex and pigment complex forms new hemoglobin. This may be illustrated graphically as follows:



The statement is true that bile pigments are formed when blood destruction results in the consequent liberation of hemoglobin, but the amount of bile pigment is not dependent upon the amount of red cell destruction. Several billion red cells would have to be destroyed daily to account for the amount of bilirubin daily excreted in the bile, and in those cases where the bile pigments are greatly increased there would soon be no red cells remaining in circulation. The most likely source of the bile pigment outside of red cell destruction is the liver, and to strengthen this belief is the fact that in Eck[2] fistula dogs, in which the liver is known to have diminished function, the pigment output is lessened 30 to 50 per cent.

Furthermore,[3] it is well established that in dogs the bile pigment excretion may be increased 50 per cent. by changing

[1] G. H. Whipple: Arch. Int. Med., 29, 711, June, 1922.
[2] Whipple and Hooper: Amer. Jour. Physiol., 42, 544, 1917.
[3] Ibid., 40, 349, 1916.

the regular meat diet to one of carbohydrates. This may be repeated time after time and can hardly be ascribed to red cell destruction.

Another interesting point is that bilirubin may be formed in the vessels themselves with the liver completely extruded. Bilirubin has been found in the vessels of the head and neck of dogs within two hours after the liver has been thrown out of circulation. The vessel endothelium and Kupffer cells may be responsible for this phenomenon.

In any discussion of pigment metabolism the subject of jaundice naturally arises.[1] The differentiation of obstructive and non-obstructine jaundice is of great clinical importance. True obstructive jaundice with a definite duct block is often confused with jaundice due to hemolytic processes and functional liver derangements. Acute catarrhal jaundice is included in this latter class and is considered to be a condition in which, although the ducts are swollen and occluded, there is a general cell involvement of the liver and the bile-ducts are occluded by cells which are the products of an inflammatory process.

The jaundice of hemolysis usually appears more quickly than that due to obstruction; the spleen is usually enlarged and comparatively soft, and the obstruction when present is within the acini, while in obstructive jaundice the block is between the acini. Finally, the resistance of the red blood-cells is diminished in the hemolytic type. Of course, symptomatic features, such as the onset, the character of pain, and the degree of toxicity, must also be considered.

Hijmans Van den Bergh[2] has developed a chemical method by which this differentiation may be made with accuracy and with little difficulty. That is, obstructive jaundice due to carcinoma, common duct stone, hepatic cirrhosis, and obstruction in the hepatic fissure may be easily differentiated from hemolytic and acholuric jaundice, and also functional jaundice, such as that due to catarrhal conditions and to toxic causes, as pneumonia, typhoid fever, and influenza.

[1] Jones, C. M.: Arch. Int. Med., 29, 643, May, 1922.

[2] Van den Bergh, Hijmans: Presse Medical, 1921, No. 14, p. 44.

He utilizes the fact that with Ehrlich's diazo reagent minute traces of bilirubin can be detected in the blood-serum.

Technic.—Solution A. Sulphanilic acid, 1 c.c.
Concentrated HCl, 15 "
Distilled water, 1000 "
Solution B. Sodium nitrite, 0.5 "
Distilled water, 100 "

1. Freshly mix 25 c.c. of solution A and 0.75 c.c. of solution B.

2. To 1 c.c. of this reagent add 1. c.c. of blood-serum.

Reaction 1. *Immediate* or *direct:* This begins instantly and is maximal in ten to thirty seconds, a *bluish-violet* color.

2. *Delayed:* This occurs in from one to fifteen minutes and is a *reddish* color, which gradually deepens.

Interpretation: If the direct reaction occurs it is significant of obstructive jaundice.

Reaction 3. If the direct reaction does not occur, proceed as follows: A. To 1 c.c. of blood-serum add 2 c.c. of 96 per cent. alcohol; centrifuge until albuminous precipitate has been thrown to the bottom of the tube and a clear supernatant fluid remains.

B. To 1 c.c. of supernatant fluid add 0.25 c.c. of the reagent.

Reaction: A *violet red* color, present at once.

Interpretation: When the direct reaction does not occur, but after the precipitation with alcohol the violet red color appears immediately, it is significant of hemolytic or functional jaundice.

Explanation[1]: The bilirubin in the blood-serum differs in the two conditions. In the obstructive type it is free and uncombined, while in the hemolytic type it is bound to the albuminous material and only liberated when alcohol is added.

CASE REPORTS

Case I. A female, aged twenty-four, several weeks after an attack of tonsillitis became jaundiced. There was slight febrile reaction, signs of intestinal indigestion, and some tenderness in the right upper quadrant of the abdomen. The feces were clay colored and bile was present in the urine.

[1] McNee, J. W.: British Med. Jour., May 6, 1922.

Van den Bergh Test.—Direct reaction was negative. Delayed reaction was negative. With the alcohol precipitation the violet red color was present at once.

Interpretation: The case is one of functional jaundice.

Later History.—With duodenal intubation, bile drainage was re-established and the jaundice gradually lessened; the stools became colored and the bile disappeared from the urine. She was discharged two weeks later, practically well.

Diagnosis.—Acute catarrhal jaundice.

Case II.—Female, aged twenty-eight. The illness was of eight months' duration, during which time there were attacks of jaundice of varying degree associated with hemoglobinuria. There was a marked secondary anemia; the lowest count was Hb. 19 per cent. Red blood-cells, 1,200,000; white blood-cells, 11,000; polynuclears, 60 per cent.; small lymphocytes, 32 per cent.; large mononuclears, 2 per cent.; transitionals, 4 per cent.; eosinophils, 2 per cent. There was some degenerative change in the red cells, but no primitive cells were found. The resistance of the red cells was decreased. The spleen was slightly enlarged but firm, and there was tenderness over the gall-bladder. The bile obtained by duodenal intubation was dark and viscid, but no organisms were demonstrated.

Van den Bergh Test.—The direct reaction was negative. The delayed reaction was negative. The alcoholic precipitation was positive.

Interpretation: Non-obstructive jaundice.

Subsequent History.—By repeated blood transfusions the blood was brought to Hb. 68 per cent.; red cells, 3,860,000, and a splenectomy was performed. The jaundice and hemoglobinuria cleared following operation.

Diagnosis.—Acquired hemolytic jaundice.

Case III.—A male, aged thirty-six, was seized with sudden severe epigastric pain, following which jaundice rapidly developed. He had several attacks of colicky pain in right upper abdominal quadrant and was quite tender in this region. His stools

were clay colored. There was quite a febrile reaction, but before operation the temperature had returned to normal.

Van den Bergh Test.—The direct reaction was positive. The delayed reaction was negative. The alcoholic precipitation was positive.

Interpretation: Obstructive jaundice.

Operation showed marked cholecystitis. Many gall-stones. Greatly dilated common duct.

Case IV.—A female, aged forty, was deeply jaundiced after an attack of pain in the right upper abdominal quadrant. Her temperature was 102° F., pulse 92. She vomited at frequent intervals and her stools were acholic.

Van den Bergh Test.—The direct reaction was positive. The delayed reaction was negative. The reaction with alcoholic precipitation was positive.

Interpretation: Obstructive jaundice.

Operation.—Empyema of the gall-bladder. Stones in cystic and common ducts.

Case V.—A male, aged sixty-five, had deep jaundice which had been increasing over a long period. He had frequent gastric symptoms and there was a mass in the epigastrium.

Van den Bergh Test.—The direct reaction was positive. The delayed reaction was negative. The alcoholic precipitation was positive.

Interpretation: Obstructive jaundice.

Necropsy Report.—Carcinoma of the head of the pancreas. Metastasis to the liver. The gall-bladder and intrahepatic ducts were greatly distended.

These 5 cases were chosen as typical of a large number of reactions. It can be seen that in obstructive jaundice the direct and the alcoholic precipitation reactions are both positive, while in the hemolytic and functional type the direct reaction is negative and the alcoholic precipitation positive. The test is not difficult to perform, and the interpretation becomes easy after a little experience in judging the color reactions. It is best to

choose a case that has a fairly deep jaundice when the first few tests are attempted.

Although this test is comparatively new and not tried in a sufficiently large number of cases to give it the final mark of approval, in all the cases where it has been used the results have been clear cut in the great majority. The test, we believe, will prove of great value with its increased use.

I am indebted to Mr. David Metheney for technical assistance in the cases presented.